"FETAL HEMOGLOBIN AND ALPHA 1 MICROGLOBULIN AS BIOCHEMICAL MARKERS IN PREDICTING PREECLAMPSIA IN LATE FIRST TRIMESTER AND EARLY SECOND TRIMESTER OF PREGNANCY"

Dissertation submitted to

The Tamil Nadu Dr. M.G.R Medical University

In partial fulfillment of the requirement for the award of the Degree of

M.S. OBSTETRICS AND GYNAECOLOGY

BRANCH II

THE TAMIL NADU Dr. M.G.R MEDICAL UNIVERSITY

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY,

GOVERNMENT HOSPITAL FOR WOMEN & CHILDREN,

MADRAS MEDICAL COLLEGE.

APRIL-2018

BONAFIDE CERTIFICATE

This is to certify that this dissertation entitled **"FETAL HEMOGLOBIN AND ALPHA 1 MICROGLOBULIN AS BIOCHEMICAL MARKERS IN PREDICTING PREECLAMPSIA IN LATE FIRST TRIMESTER AND EARLY SECOND TRIMESTER OF PREGNANCY"** is the bonafide original work done by **Dr.I.INBA PRIYANKA**, post graduate in the Department of Obstetrics and Gynaecology, under the guidance of **Dr.S.VIJAYA, MD, DGO.,** Professor, Institute of Social Obstetrics and Gynaecology, Kasturba Gandhi Hospital, Madras Medical College, Chennai, towards partial fulfilment of the requirement of the Tamil Nadu Dr. M.G.R Medical University for the award of M.S Degree in Obstetrics and Gynaecology, April 2018. The period of post graduate study is from June 2015 to June 2018.

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DECLARATION

I solemnly declare that this dissertation **"FETAL HEMOGLOBIN AND ALPHA 1 MICROGLOBULIN AS BIOCHEMICAL MARKERS IN PREDICTING PREECLAMPSIA IN LATE FIRST TRIMESTER AND EARLY SECOND TRIMESTER OF PREGNANCY"** was prepared by me under the guidance and supervision of **Dr.S.VIJAYA, MD, DGO.,** Professor, Institute of Social Obstetrics and Gynaecology, Kasturba Gandhi Hospital, Madras Medical College, Triplicane, Chennai.

This dissertation is submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Chennai** in partial fulfillment of the University regulations for the award of the degree of **M.S. (Obstetrics and Gynaecology).**

Place: Chennai

Date: **DR.I.INBA PRIYANKA**

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I am immensely grateful to all the patients who took part in the study.

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CERTIFICATE OF APPROVAL

To
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Dear Dr.I. Inba Priyanka,

The Institutional Ethics Committee has considered your request and approved your study titled **"FETAL HEMOGLOBIN AND ALPHA 1 MICROGLOBULIN AS BIOCHEMICAL MARKERS IN PREDICTING PRE ECLAMPSIA IN LATE FIRST TRIMESTER AND EARLY SECOND TRIMESTER OF PREGNANCY " NO. 29102016.**

The following members of Ethics Committee were present in the meeting hold on **04.10.2016** conducted at Madras Medical College, Chennai 3

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2.Dr.M.K.Muralidharan,MS.,M.Ch.,Dean, MMC,Ch-3	:Deputy Chairperson
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10.Thiru S.Govindasamy, BA.,BL,High Court,Chennai	: Lawyer
11.Tmt.Arnold Saulina, MA.,MSW.,	:Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

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TABLE OF CONTENTS

INTRODUCTION

Preeclampsia is a systemic syndrome manifesting as “new onset hypertension and proteinuria after 20 weeks of gestation” occurring in about 3 to 5% of pregnant women Preeclampsia is a complex clinical syndrome with hypertension representing as the major manifestation. Pathogenesis of preeclampsia include defective perfusion of maternal spiral arteries by the trophoblast, endothelial injury leading to activation of coagulation, secretion of endothelial cell toxin, altered endothelial permeability and impairment of vasodepressor function. These changes lead to the clinical manifestation of preeclampsia. The primary biochemical, immunologic and genetic basis of preeclampsia remains speculative.

However recent studies here indicated the involvement of hemoglobin induced oxidative stress in the development of preeclampsia. The oxidative stress may damage the blood placenta barrier leading to elevated levels of HbF in maternal plasma or serum. In addition, marker for oxidative stress such as antioxidant endogenous protein α1 microglobulin were found to be elevated.

In this background the present study is undertaken to assess the levels of fetal hemoglobin and α1 microglobulin in late first and early second trimester and to determine whether they can be used as predictive markers for preeclampsia.

AIMS AND

OBJECTIVES

To establish association between high levels of fetal hemoglobin and alpha 1 microglobulin in plasma of pregnant womenin 10 to 16 weeks of gestational age and subsequent development of preeclampsia.

REVIEW OF LITERATURE

Hypertensive disorders are one of the most common medical disorders of pregnancy. It has an incidence between 5 to 10%.

About 20% of fetal deaths and 30% of maternal death are due to hypertensive disorders of pregnancy. The major focus of research in obstetrics is to identify mothers who are at risk of adverse pregnancy outcome.

EPIDEMIOLOGY AND RISK FACTORS

Hypertensive disorders complicate nearly 7.5% of nulliparous women. Even though preeclampsia occurs mainly in the nulliparous women, there is increased risk of preeclampsia in multiparous women with a new partner which is similar to that of nulliparous women. Increased interpregnancy interval and change in paternity may increase the risk of developing preeclampsia. Increased incidence is also due to postponement of first pregnancy to a later age and increased prepregnancy weight.

A women who has developed preeclampsia is at increased risk of developing the same in subsequent pregnancies. Diabetes, renal diseases, chronic hypertension, hypercoagulable states are some disorders that increase the risk of preeclampsia. Multifetal pregnancy and hydatiform mole have large placental mass and increase the chance of preeclampsia. Smoking provides protection against development of preeclampsia.

DEFINITION

Hypertension is defined as systolic blood pressure equal to or greater than 140 mmof Hg and / or diastolic blood pressure of 90mm of Hg or more measured on two occasions at least 4 hours apart within 7 days beyond 20 weeks of gestation.

National high blood pressure education programme (2000) categorized hypertensive disorders in pregnancy as follows

1. Gestational hypertension
2. Preeclampsia
3. Eclampsia
4. Chronic hypertension
5. Superimposed preeclampsia on chronic hypertension

GESTATIONAL HYPERTENSION

Gestational hypertension is diagnosed in a pregnant women when the blood pressure is 140/90 mm of Hg or greater after 20 weeks of gestation which returns back to normal by 12 weeks postpartum without proteinuria.

Chronic hypertension is diagnosed, if blood pressure remains elevated beyond 12 weeks postpartum. When gestational hypertension develops before 35 weeks of gestation, there is increased chance of patient developing preeclampsia.

PREECLAMPSIA

Preeclampsia is defined as " onset of hypertension after twentieth week of gestation, along with proteinuria. Proteinuria is confirmed if there is > 300mg of protein in 24 hours urine collection or a urinary dipstick shows >= +2 or protein/ creatinine ratio more than 0.3.

Preeclampsia complicates 2 to 8% of pregnancies. ACOG removed proteinuria as a criteria for diagnosing preeclampsia in 2013. When preeclampsia develops before 34 weeks but after 20 weeks of gestation, it is called early onset preeclampsia.

Preeclampsia is diagnosed in the absence of proteinuria when the patient develops any one of the following along with new onset hypertension

1. Platelets < 1,00,000/mm3
2. Elevated aspartate transaminase or alanine transaminase atleast twice normal concentrations
3. Serum creatinine > 1.1 mg/dl
4. Microangiopathic hemolysis
5. Persistent headache or other cerebral or visual disturbances
6. Persistent epigastric pain / right upper quadrant pain

Severe preeclampsia is termed when blood pressure is

> 160/110mm of hg with signs and symptoms of end organ damage.

ECLAMPSIA

Convulsions that cannot be attributed to other causes and/ or unexplained coma during pregnancy or puerperium ina woman with preeclampsia.

CHRONIC HYPERTENSION

Hypertension diagnosed before 20 weeks of gestational age or after 20 weeks of gestation and persistent beyond 12 weeks postpartum or whichever is diagnosed before pregnancy.

SUPERIMPOSED PREECLAMPSIA ON CHRONIC HYPERTENSION

A sudden increase in blood pressure, proteinuria or < 1 lakh platelet count in hypertensive women and proteinuria before 20 weeks gestation or a new onset proteinuria in hypertensive women after 20 weeks of gestation age.

IMPENDING ECLAMPSIA

The following are the signs and symptoms of impending eclampsia

-Persistent headache

-Visual disturbances

-Oliguria

-Nausea/vomiting

-Epigastric pain

-Restlessness/agitation

-Coagulatory disturbances

CLINICAL FEATURES

Preeclampsia is a condition which is difficult to diagnose due to its variety of presentations and lack of a specific diagnostic test.

Preeclampsia is diagnosed when a pregnant women develops hypertension(systolic blood pressure >=140 mm of Hg or diastolic blood pressure >=90mm of Hg) and proteinuria (300mg or greater in 24 hr urine sample) after 20 weeks of gestation.

About 20% of women with atypical preeclampsia have minimal or no proteinuria.

Previously preeclampsia is characterised by hypertension, proteinuria, and oedema. However oedema isno longer considered for diagnosis. Currently preeclampsia is divided into mild and severe preeclampsia. Headache, blurring of vision, epigastric/right upper quadrant pain, oliguria, hemolysis, pulmonary oedema, platelet count<1,00,000mm3 are signs of severe preeclampsia.

HELLP syndrome include hemolysis, elevated liver enzymes and low platelet count. It is a severe form of the disease and indicate immediate delivery.

Fetal complications caused by preeclampsia include oligohydramnios, IUGR, iatrogenic prematurity and perinatal death.

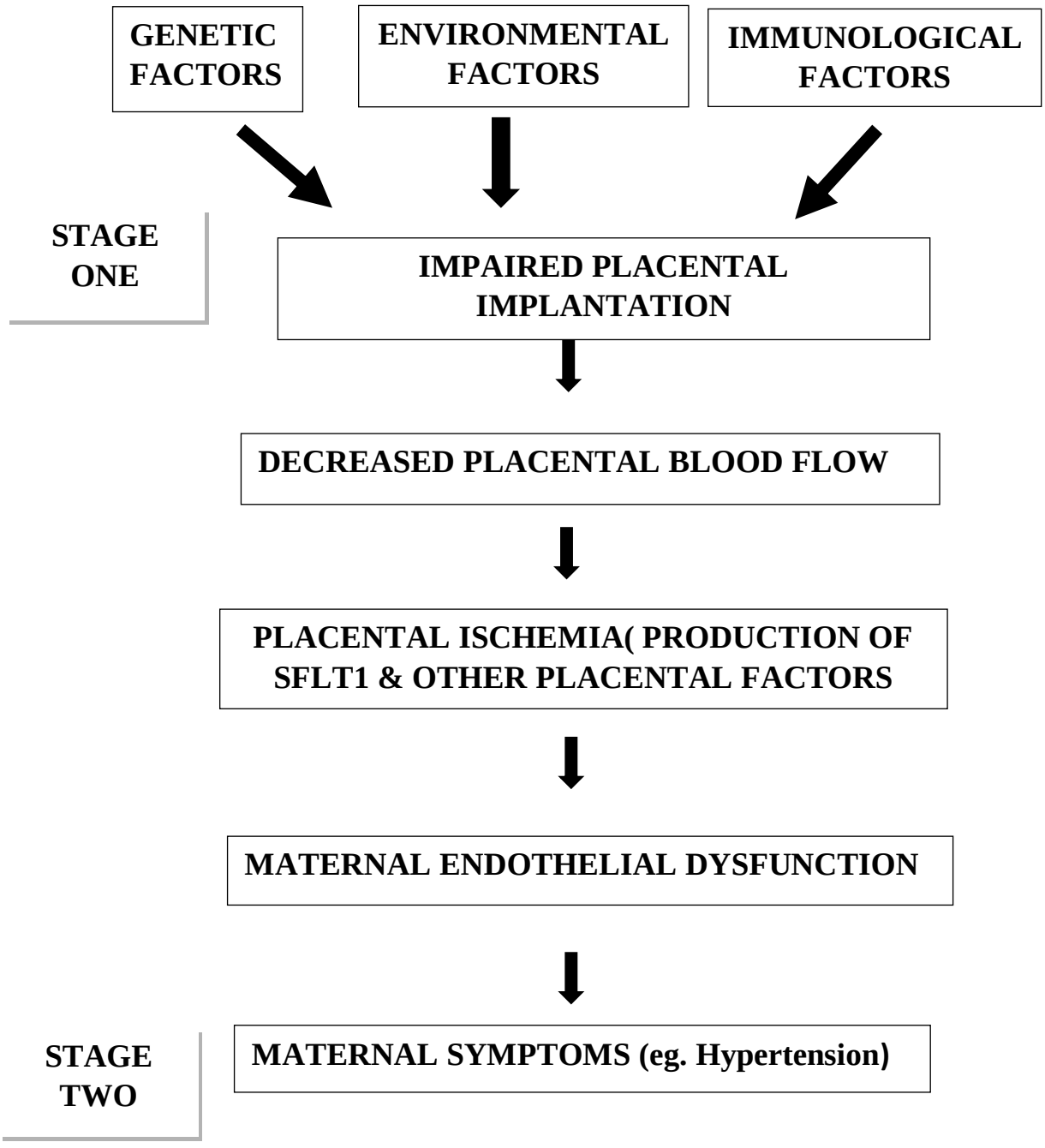
Eclampsia develops in 2% of women with preeclampsia. Eclamptic seizures is more common in immediate postnatal period. But seizures can also occur from 48 hours postpartum to one month postpartum. Nearly one third patients with postpartum eclamptic seizures have never shown any signs of preeclampsia during pregnancy.

LONG TERM MATERNAL COMPLICATIONS

It has been believed that with the delivery of the placenta, complication of preeclampsia resolve. But new research suggests that risk to the mother persists long after her reproductive years are over. The risk of cardiovascular and cerebrovascular is doubled in woman with preeclampsia and gestational hypertension. 20% of preeclamptic women develop hypertension within 7 years of pregnancy.

PATHOGENESIS

The pathophysiology of preeclampsia starts from the placenta. Preeclampsia is described as a two stage syndrome.



Newer techniques like proteomics and genomics have revealed fetal HbF as a potential factor linking stage 1 and 2 in preeclampsia. The analyses have revealed an accumulation of fetalHbF in placental vascular lumen. The cells which express HbF have identified as hematopoietic stem cells located close to lumen.

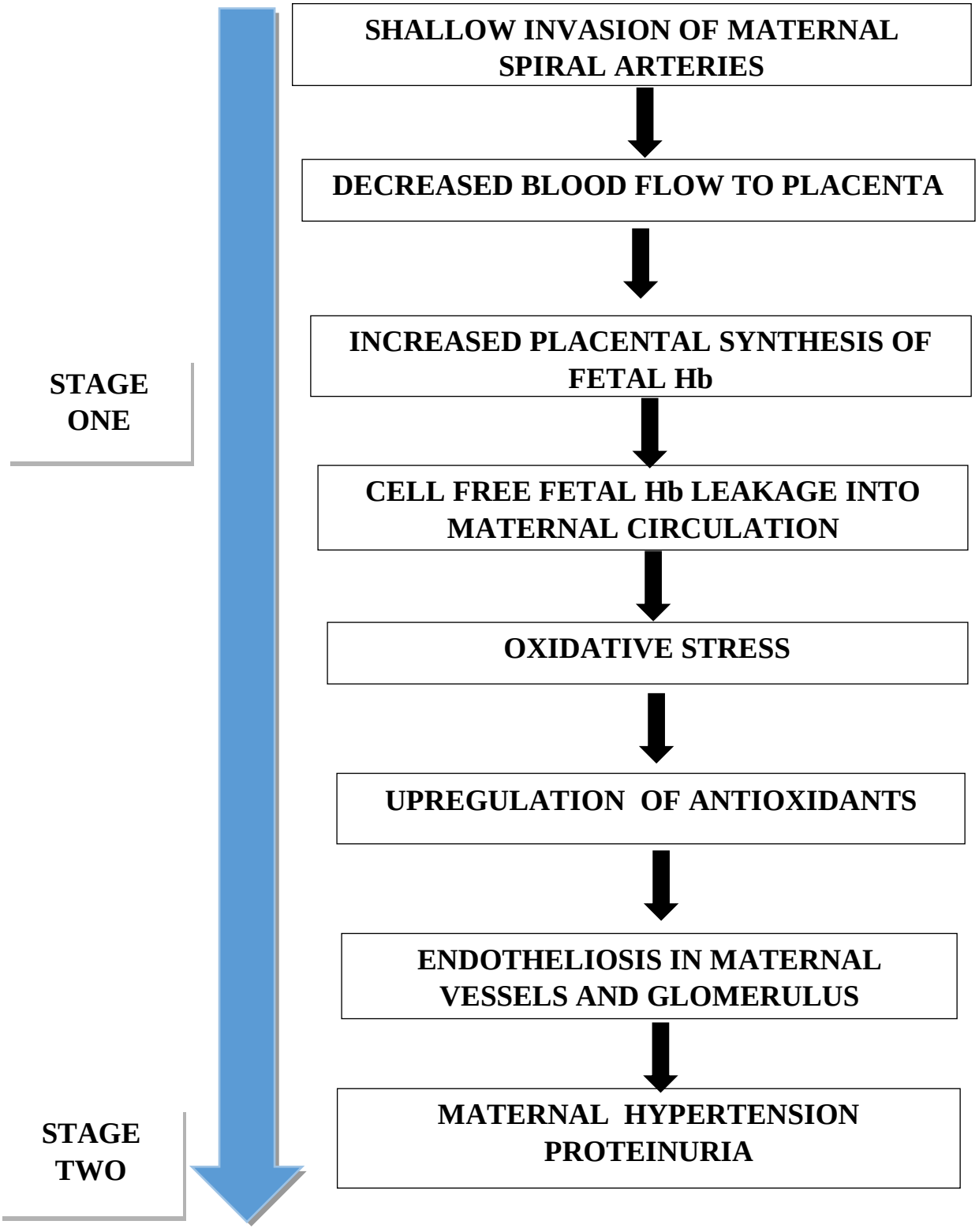
Cell free hemoglobin and its metabolites are toxic to tissue since they cause oxidative stress which is an imbalance between reactive oxidative compounds and physiological antioxidative defence mechanisms. Antioxidants inhibit oxidation. Alpha 1 microglobulin is a protein which has both enzymatic and non enzymatic antioxidant properties.

In preeclampsia, oxidative stress occurs in both placenta and maternal circulation. Extracellular Hb induces oxidative stress at a very high level. The cell Hb binds to nitric oxide and causes vasoconstriction which leads to increased blood pressure.

In order to protect the body against harmful effects of free Hb, a range of physiological defence mechanisms have evolved. Cell free Hb is bound to haptogloblin while Hb metabolite heme to hemopexin, albumin, alpha 1 microglobulin.

Alpha 1 microglobulin is a plasma protein that provides protection due to its ability to bind and neutralize free heme and radicals. Several studies have shown that there is upregulation of A1M expression in liver and placenta following exposure to Hb. The serum concentration of A1M have been shown to be significantly elevated in maternal blood in first trimester for pregnant women subsequently developing, preeclampsia.

Modified two stage model on basis of HbF hypothesis



PATHOPHYSIOLOGY

ABNORMAL PLACENTATION

In normal pregnancy, there is controlled trophoblastic invasion from the decidua up to the inner third of the myometrium thus the endothelial and muscular layer of spiral arteries are disrupted converting the small muscular arteries to large capacity low resistance vascular spaces a process called pseudovascularization. It occurs in 2 stages. First occurs before 12 weeks of GA upto the interface between decidua and myometrium. Second stageoccurs between 12 & 16 weeks and invades spiral arteries in the intramyometrial segment.

In preeclampsia, there is decreased or absent second wave of trophoblastic invasion of maternal spiral arteries as compared to normal pregnancy.

MATERNAL ENDOTHELIAL DYSFUNCTION

Placenta is the organ of origin in preeclampsia. However, maternal endothelium is the organ of target. The released vasopressive factors from placenta cause damage to endothelium of maternal organs. In normal pregnancy, decrease in blood pressure and vascular resistance occurs. In preeclampsia, systemic vascular resistance is high & cardiac output is low due to generalized vasoconstriction.

PRO AND ANTI-ANGIOGENIC FACTORS

The vascular development in placenta involves several pro and anti angiogenic factors .They include

- VEGF (Vascular Endothelial Growth Factor)
- PGF (Placental Growth Factor)
- SFLt-1 (Soluble fms like tyrosine kinase – 1)
- Soluble endoglin

Imbalance in these factors may result in endothelial dysfunction.

RENIN ANGIOTENSIN ALDOSTERONE SYSTEM

Pregnant women usually have response to the effects of Angiotensin II. In patients with preeclampsia aldosterone level is increased in 3rd trimester. In addition the refractoriness to angiotensin II is also lost in the second trimester, This is because in normal pregnancy there is down regulation of angiotensin receptors. But in preeclamptic women, there is elevated levels of angiotensin receptors.

OXIDATIVE STRESS

In the preeclamptic women there is an increase in serum lipid peroxide levels which causes cellular damage. The oxidative stress causes increase in capillary permeability leading to oedema, proteinuria and microvascular coagulation .

HEMATOLOGICAL CHANGES

Due to endothelial damage there is leakage of plasma into interstitial space causing decreased blood volume. These patients have thrombocytopenia, hemolysis and deranged coagulation profile depending on the severity of the disease.

CARDIOVASCULAR CHANGES

There is increased peripheral resistance and decreased cardiac output. Pulmonary wedge pressure and central venous pressure are reduced in preeclampsia**.**

HEPATIC CHANGES

Hepatic changes include hemorrhage, peripheral fibrin deposition, areas of infarction and necrosis. The subscapular hemorrhages which occurs in liver gives it a mottled appearance. The subcapsular hemorrhage causes right upper or epigastricpain .

RENAL CHANGES

In the pre eclamptic women, changes like glomerular enlargement, focal segmental glomerular sclerosis, swelling of mesangium, endothelial cell hyperplasia, sub endothelial fibrinoid deposition occur. Glomerular filtration rate and renal plasma flow are reduced in pre eclampsia.

CHANGES IN BRAIN

The most common finding in brain is oedema due to both increased vasospasm of cerebral arterioles and over dilatation of vessels due to failure of autoregulatory mechanism of brain. Changes are most commonly seen in posterior hemisphere causing visual disturbances like scotoma, blurring of vision and diplopia .

MATERNAL COMPLICATIONS

- Eclampsia

-HELLP (Hemolysis, Elevated Liver enzymes, Low platelets)

-Pulmonary edema

-Disseminated Intravascular coagulopathy

-Hypertensive Encephalopathy

-Acute renal failure

FETAL COMPLICATIONS

- Intrauterine fetal growth restriction
- Preterm birth
- Oligohydramnios
- Intrauterine death

HELLP SYNDROME

The term ‘HELLP’ was coined by Weinstein in 1982 .

H – Hemolysis

EL – Elevated liver Enzymes

LP – low platelets

Hemolysis is defined as presence of abnormal peripheral smear with schistocytes, total bilirubin level more than 1.2 mg/dl, liver enzymes are elevated when aspartate aminotransferase is more than 70U/L and LDH more than 600 U/L .When platelets are less than 1,00,000/ mm3 it is called low platelet count.

Martin el al categorized HELLP Syndrome into three classes based on platelet count (Mississipi scoring). Class 1 is defined as platelet count less than 50,000/mm3. Class 2 as platelet count less than 50,000 to 1,00,000/mm3 and class 3 as platelet count more than 1,00,000/mm3.

MANAGEMENT

The only definitive treatment of preeclampsia is termination of pregnancy.

Management depends on the severity of the disease and the period of gestation.

Elective induction of labour is done when the gestational age is 37 weeks or more.

In severe pre eclampsia,34 weeks is taken as the cut off for termination of pregnancy.

However when severe preeclampsia is not responding to treatment, termination of pregnancy is offered after a course of steroids, before 34 weeks.

MANAGEMENT OF SEVERE PREECLAMPSIA ACCORDING TO GESTATIONAL AGE

<24 weeks – Stabilise the patient and terminate

25-33 weeks-Expectant management and maternal and fetal monitoring, steroids given for lung maturity of fetus.If there is maternal or fetal indication then terminate the pregnancy.

>34 weeks-Stabilise the patient with fetal monitoring and then deliver.

ANTIHYPERTENSIVE THERAPY

The blood pressure at which antihypertensive should be started is still controversial.Antihypertensive should be started in case of severe hypertension (ie) diastolic pressure >110 mm of Hg and / or systolic pressure >160 mm of Hg to prevent maternal and fetal complications.

Recent guidelines indicate antihypertensive treatment for mild preeclampsia(140-159/90-109 mm of Hg) to maintain systolic BP at 130-155 and diastolic BP at 80-105 mm of Hg.

First line drugs for antihypertensive therapy are labetolol, nifedipine and alpha methyl dopa.

Reducing maternal BP does not have effect on fetus, but may reduce fetal perfusion and may indirectly affect the fetal growth.

LABETOLOL

It is an alpha and beta blocker. Used as first line therapy in pregnancy oral drug given as 100-400 mg twice daily.

For severe preeclampsia iv dose of 10-20 mg given initially followed by 20-80 mg every 30 minutes upto a maximum dose of 300 mg

ALPHA METHYL DOPA

It is a centrally acting alpha adrenergic agonist.It decreases the sympathetic tone and arterial blood pressure.

It is given as a dose of 250-500 mg orally two to three times a day upto a maximum dose of 2 g.

NIFEDIPINE

It is a calcium channel blocker. It is given as a dose of 10-20 mg three to four times daily with a maximum dose of 120 mg/day.

ECLAMPSIA MANAGEMENT

The management of eclampsia includes

1) Clearing airways
2) Control of seizures (MgSO4 regimen)
3) Control of BP
4) Delivery of baby
5) Postpartum monitoring

MgSO4 REGIMEN (ZUSPAN REGIMEN is followed in my Institution)

Loading dose: 4 g of 20% MgSO4 given over 15 – 20 minutes

Maintenance dose: 1g/hr of MgSO4 is infused. It is discontinued after 24 hours of delivery or last convulsions whichever is last.

CONTRACEPTION

Postpartum IUCD may be inserted in preeclamptic women. Progesterone only pills may be prescribed at 6 weeks postpartum when BP is found to be normal.

When BP remains elevated, followup at 12 weeks postpartum required and women may be offered IUCD or condoms.

MATERIALS AND METHODS

The present study was undertaken in the Department of Obstetrics and Gynaecology, between September 2016 and august 2017. This was a prospective cohort study done to establish association between high levels of fetal hemoglobin and alpha 1 microglobulin in pregnant women of 10 to 16 weeks of GA and subsequent development of preeclampsia in these women.A total of 100 pregnant women were included in the study.

INCLUSION CRITERIA:

-10 – 16 weeks of pregnancy

-Singleton /Multiple pregnancy

-Age 20-35 years

-Both primi and multigravida

-BMI 16-35

EXCLUSION CRITERIA

-Diabetes

-Hypertension

-Renal disease

-Epilepsy

-Vascular disorders

PARAMETERS STUDIED:

-Fetal hemoglobin

-Alpha 1 microglobulin

PROCEDURE:

Hundred pregnant women attending IOG hospital who were willing to participate in the study were recruited after getting consent. Blood samples of these women were collected and measured using ELISA. They were managed by department protocol and followed till delivery. General parameters like age, parity, BP, BMI, gestational age, mode of delivery and perinatal outcome were compared between both groups. The values of fetal hemoglobin and α1 microglobulin were correlated with the development of preeclampsia.

STATISTICAL ANALYSIS:

Data were collected and included in a data based system and analysed by statistician. Parametric data were expressed as mean and standard deviation. It was analysed statistically using t-test and non parametric data were expressed as percentages and analyzed using chi square. Receiver operator characteristics analysis was used to identify the optimal threshold values of fetal hemoglobin and α1 microglobulin. Sensitivity, specificity, positive and negative predictive values of fetal hemoglobin and alpha 1 microglobulin were profiled by curves. All participants were subjected to full history taking and clinical examination.

Fetal hemoglobin and alpha 1 microglobulin levels were measured by ELIZA technique.

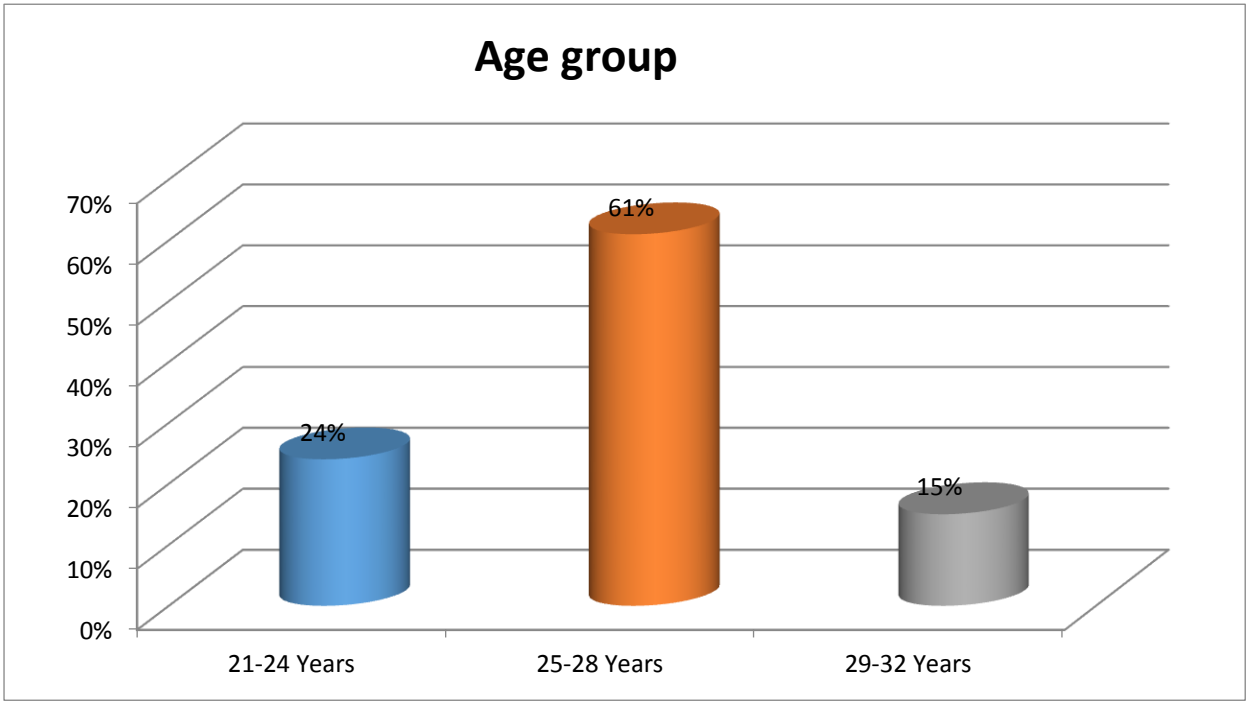
RESULTS

The present study was conducted in the department of Obstetrics and Gynaecology, from September 2016 to August 2017. One hundred women constituted the study group. Levels of fetal hemoglobin and α1 microglobulin were estimated. The results are presented below.

Frequency Table: TABLE I

Age group	Frequency	Percent
21-24 Years	24	24.0
25-28 Years	61	61.0
29-32 Years	15	15.0
Total	100	100.0

FIGURE I



In my study there were 24% women between 21-24 years,61% women between 25-28 years and 15% women between 29-32 years.

TABLE II

Cross tab

			DEVELOPED PE		Total
			No	Yes	
age group	21-24 Years	Count	9	15	24
		% within DEVELOPED PE	20.5%	26.8%	24.0%
	25-28 Years	Count	29	32	61
		% within DEVELOPED PE	65.9%	57.1%	61.0%
	29-32 Years	Count	6	9	15
		% within DEVELOPED PE	13.6%	16.1%	15.0%
Total		Count	44	56	100
		% within DEVELOPED PE	100.0%	100.0%	100.0%

Pearson Chi-Square=0.819 p=0.664

Majority of women who developed preeclampsia belong to age group of 25-28 years .However there was no statistical significance in development of preeclampsia with respect to age group.

TABLE III

			ALPHA1_GROUP		Total
			0-1.86	ABOVE 1.86	
age_group	21-24 Years	Count	9	15	24
		% within ALPHA1_GROUP	20.9%	26.3%	24.0%
	25-28 Years	Count	29	32	61
		% within ALPHA1_GROUP	67.4%	56.1%	61.0%
	29-32 Years	Count	5	10	15
		% within ALPHA1_GROUP	11.6%	17.5%	15.0%
Total		Count	43	57	100
		% within ALPHA1_GROUP	100.0%	100.0%	100.0%

Pearson Chi-Square=1.381 p=0.501

TABLE IV
Crosstab

			FETAL_GROUP		Total
			0-1.92	ABOVE 1.92	
age_group	21-24 Years	Count	9	15	24
		% within FETAL_GROUP	20.5%	26.8%	24.0%
	25-28 Years	Count	29	32	61
		% within FETAL_GROUP	65.9%	57.1%	61.0%
	29-32 Years	Count	6	9	15
		% within FETAL_GROUP	13.6%	16.1%	15.0%
Total		Count	44	56	100
		% within FETAL_GROUP	100.0%	100.0%	100.0%

Pearson Chi-Square=0.819 p=0.664

There is no statistical significance between values of fetal hemoglobin and alpha 1 microglobulin with respect to age of pregnant women.

TABLE V

PARITY	Frequency	Percent
Primi	56	56.0
Multi	44	44.0
Total	100	100.0

FIGURE II

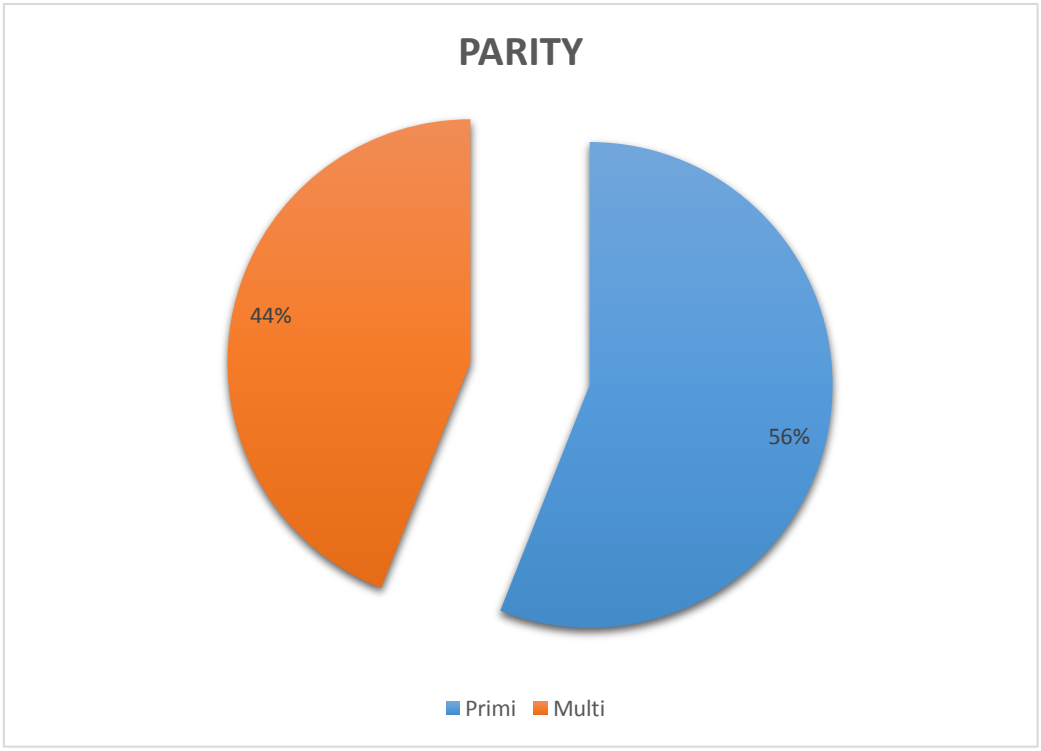


TABLE VI

PARITY * DEVELOPED_PE Cross tabulation

			DEVELOPED_PE		Total
			No	Yes	
PARITY	Primi	Count	26	30	56
		% within DEVELOPED_PE	59.1%	53.6%	56.0%
	Multi	Count	18	26	44
		% within DEVELOPED_PE	40.9%	46.4%	44.0%
Total		Count	44	56	100
		% within DEVELOPED_PE	100.0%	100.0%	100.0%

Pearson ChiSquare=0.305 P=0.581

There were 53.6% primi and 46% multi in my study. Eventhough the incidence of preeclampsia was found to be more among primi, there was no statistical significance in parity with respect to preeclampsia.

TABLE VII

BMI Group	Frequency	Percent
<18.5	16	16.0
18.5-24.99	67	67.0
25-29.99	11	11.0
ABOVE 30	6	6.0
Total	100	100.0

FIGURE III

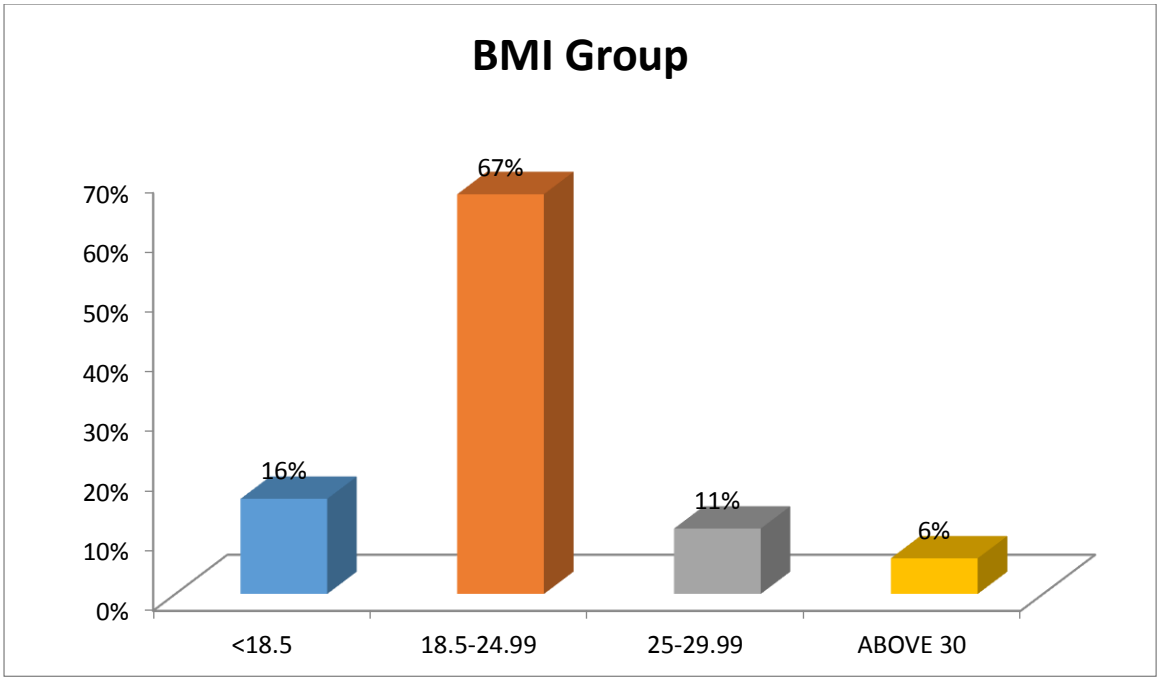


TABLE VIII

Crosstab

			DEVELOPED PE		Total
			No	Yes	
BMI GROUP	<18.5	Count	7	9	16
		% within DEVELOPED PE	15.9%	16.1%	16.0%
	18.5-24.99	Count	33	34	67
		% within DEVELOPED PE	75.0%	60.7%	67.0%
	25-29.99	Count	4	7	11
		% within DEVELOPED PE	9.1%	12.5%	11.0%
	ABOVE 30	Count	0	6	6
		% within DEVELOPED PE	0.0%	10.7%	6.0%
Total		Count	44	56	100
		% within DEVELOPED PE	100.0%	100.0%	100.0%

Pearson Chi-Square=7.969* p=0.047

Incidence of pre eclampsia was found to be more among BMI group of 18.5 to 24.99, there was no statistical significance between BMI and development of preeclampsia.

TABLE IX

Crosstab

			ALPHA1_GROUP		Total
			0-1.86	ABOVE 1.86	
BMI_GROUP	<18.5	Count	7	9	16
		% within ALPHA1_GROUP	16.3%	15.8%	16.0%
	18.5-24.99	Count	32	35	67
		% within ALPHA1_GROUP	74.4%	61.4%	67.0%
	25-29.99	Count	4	7	11
		% within ALPHA1_GROUP	9.3%	12.3%	11.0%
	ABOVE 30	Count	0	6	6
		% within ALPHA1_GROUP	0.0%	10.5%	6.0%
Total		Count	43	57	100
		% within ALPHA1_GROUP	100.0%	100.0%	100.0%

Pearson Chi-Square=5.347 p=0.148

TABLE X

Crosstab

			FETAL_GROUP		Total
			0-1.92	ABOVE 1.92	
BMI_GROUP	<18.5	Count	6	10	16
		% within FETAL_GROUP	13.6%	17.9%	16.0%
	18.5-24.99	Count	34	33	67
		% within FETAL_GROUP	77.3%	58.9%	67.0%
	25-29.99	Count	4	7	11
		% within FETAL_GROUP	9.1%	12.5%	11.0%
	ABOVE 30	Count	0	6	6
		% within FETAL_GROUP	0.0%	10.7%	6.0%
Total		Count	44	56	100
		% within FETAL_GROUP	100.0%	100.0%	100.0%

Pearson Chi-Square=8.729 * p=0.033

There was no statistical significance between levels of fetal hemoglobin and alpha 1 microglobulin and BMI of pregnant women.

FIGURE IV

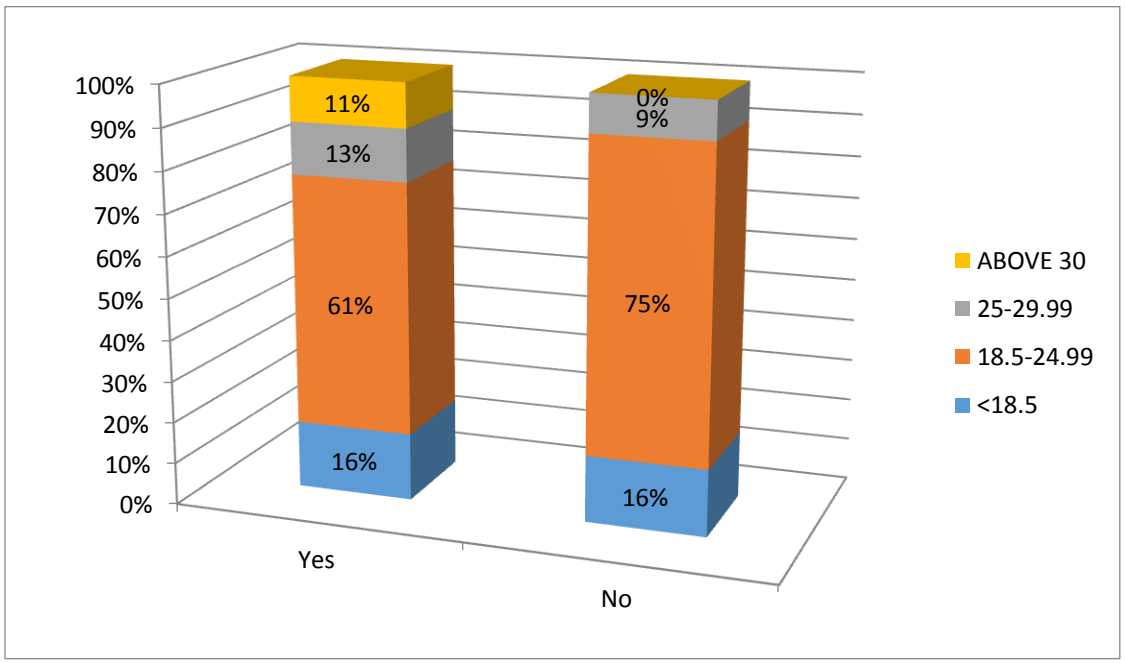
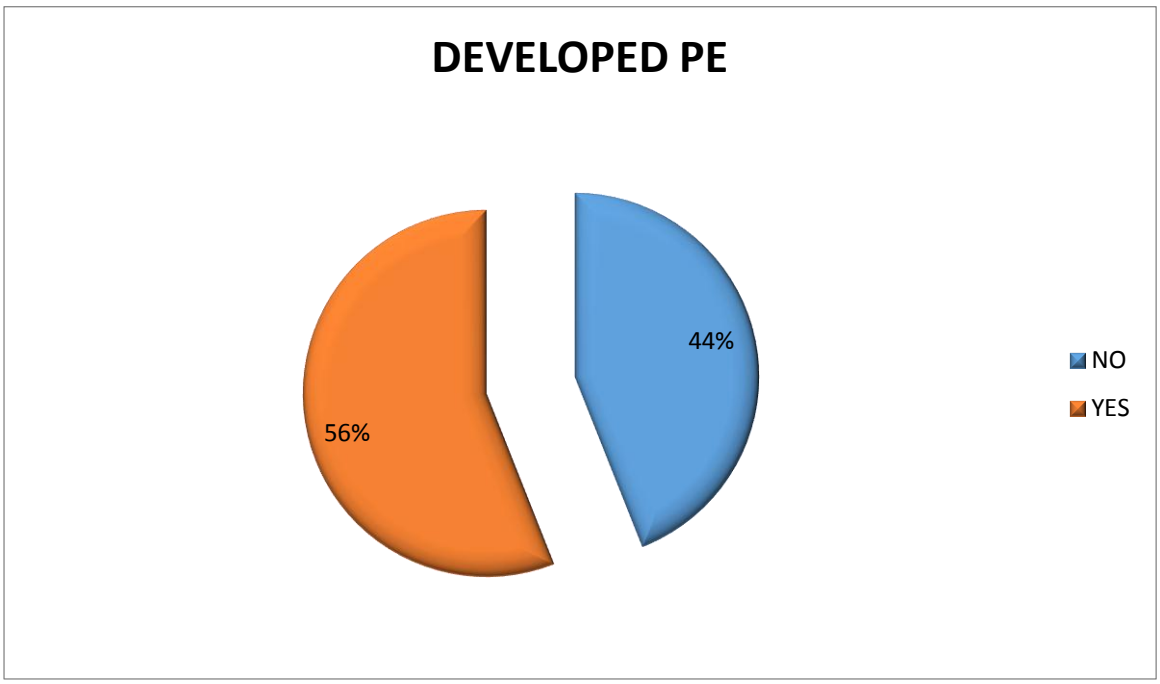


TABLE XI

DEVELOPED PE	Frequency	Percent
No	44	44.0
Yes	56	56.0
Total	100	100.0

FIGURE V



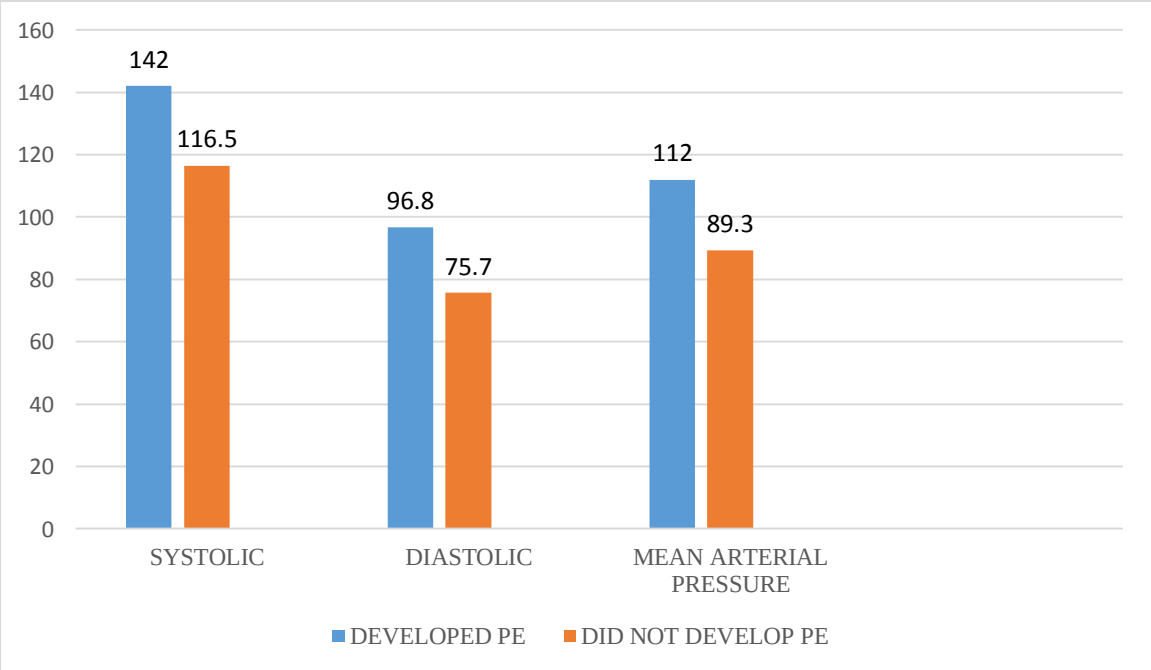
Out of hundred women, 56 women developed preeclampsia and 44 women did not develop preeclampsia.

Blood pressure at admission

TABLE XII

BLOOD PRESSURE	DEVELOPED PE	DID NOT DEVELOP PE
SYSTOLIC(mm of Hg)	142	116.5
DIASTOLIC(mm of Hg)	96.8	75.7
MEAN ARTERIAL PRESSURE(mm of Hg)	111.33	89.3

FIGURE VI



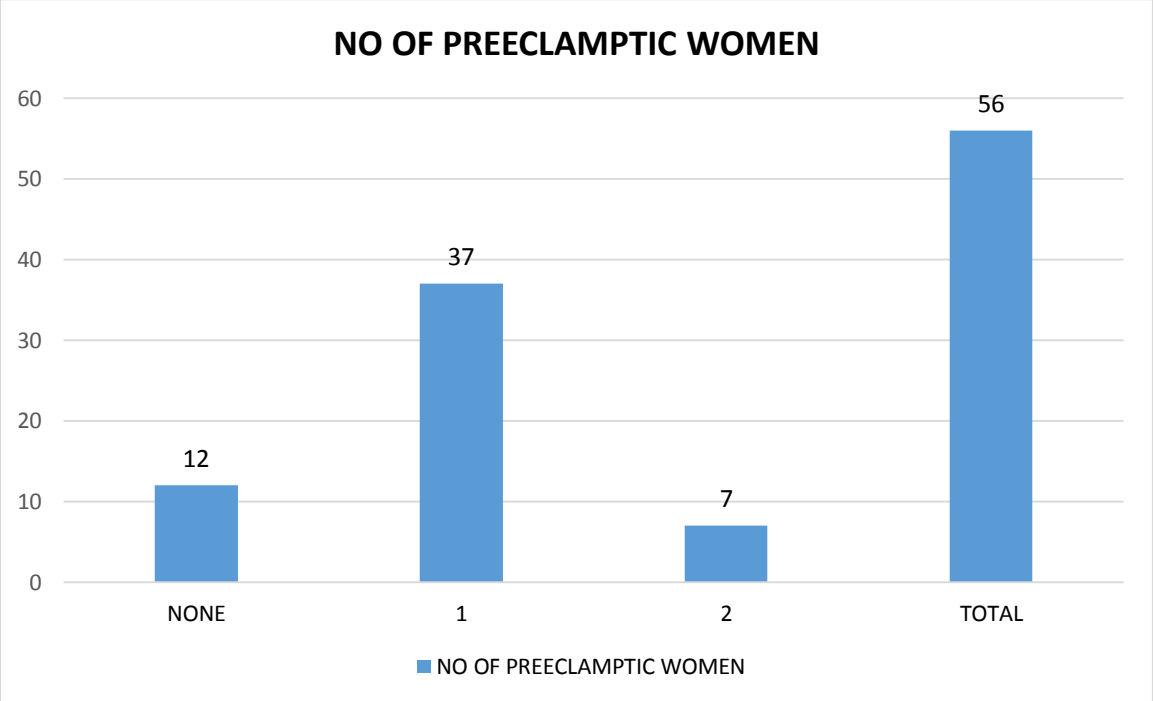
The mean sysytolic, diastolic and mean arterial pressures of preeclamptic women were elevated at the time of admission. The mean arterial pressure was 89.3 mm of Hg in normotensive women and 111.33 mm of Hg in women who developed preeclampsia.

Usage of antihypertensives (TABLE XIII)

No of Antihypertensive drugs	Preeclamptic women
NONE	12 (21.4%)
1	37 (66.1%)
2	7 (12.5%)
TOTAL	56 (100%)

In the antenatal period, all women with preeclampsia received antihypertensives for control of blood pressure. Among them, 49 required 1 antihypertensive drug and 7 required 2 antihypertensive drug.

FIGURE VII

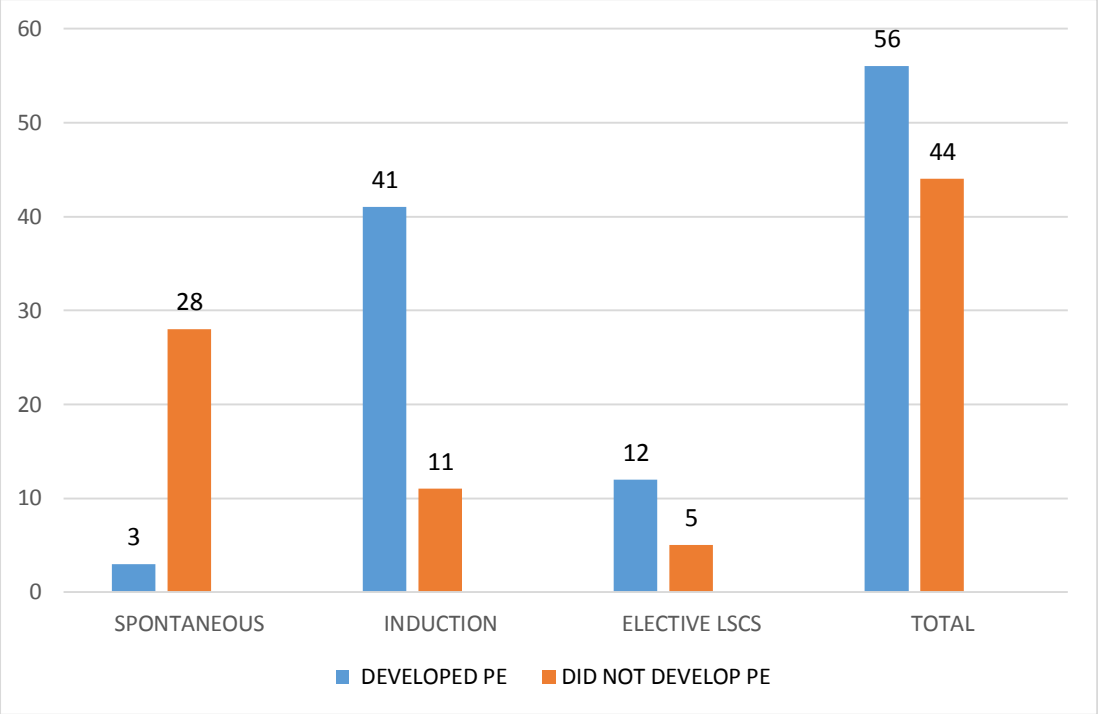


No Of Antihypertensive Drugs

Type of labour (TABLE XIV)

ONSET OF LABOUR	DEVELOPED PE	NOT DEVELOPED PREECLAMPSIA
SPONTANEOUS	3	28
INDUCTION	41	11
ELECIVE CAESEREAN	12	5
TOTAL	56	44

FIGURE VIII



The induction rate was higher in women who developed preeclampsia compared to women who did not develop pre eclampsia. Out of 56 women who had developed preeclampsia, labour was induced in 41, spontaneous onset of labour in 3 women and 12 underwent elective caesarean section.

TABLE XV: MODE OF DELIVERY

MODE OF DELIVERY	Frequency	Percent
FTNVD	62	62.0
LSCS	38	38.0
Total	100	100.0

FIGURE IX

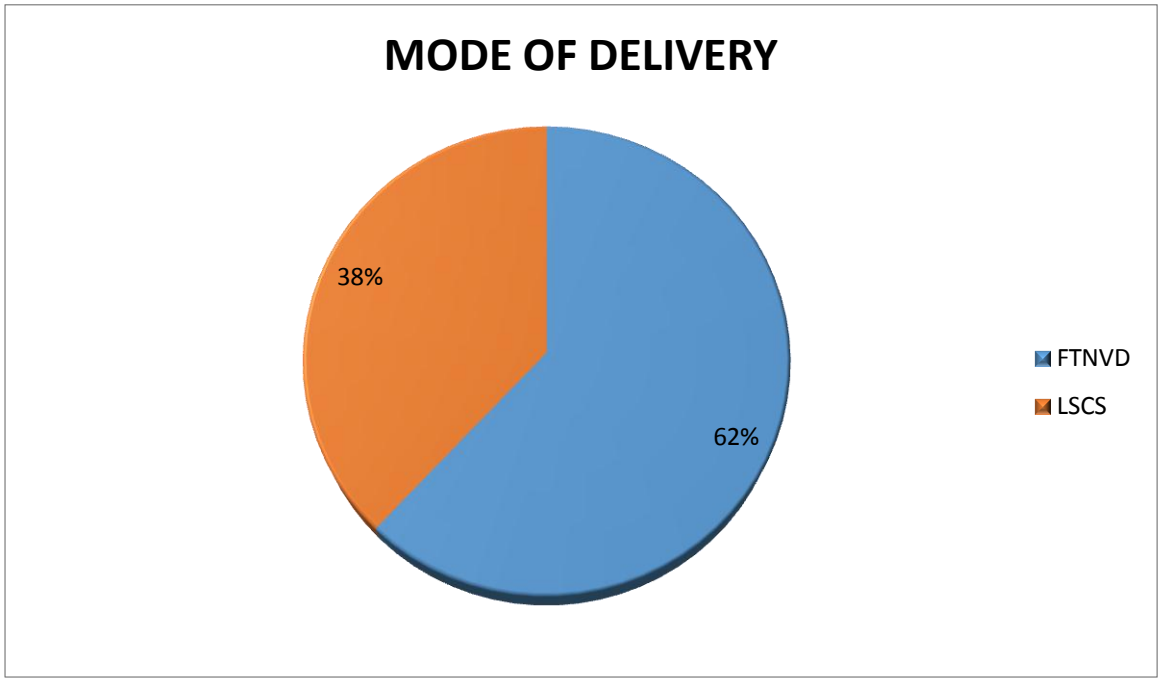


TABLE XIV

Crosstab

			DEVELOPED PE		Total
			No	Yes	
MODE OF DELIVERY	FTNVD	Count	33	29	62
		% within DEVELOPED PE	75.0%	51.8%	62.0%
	LSCS	Count	11	27	38
		% within DEVELOPED PE	25.0%	48.2%	38.0%
Total		Count	44	56	100
		% within DEVELOPED PE	100.0%	100.0%	100.0%

Pearson Chi-Square=5.636* p=0.018

There was no statistical significance between mode of delivery and development of pre eclampsia.

MODE OF DELIVERY IN WOMEN WHO DEVELOPED PREECLAMPSIA

	COUNT	PERCENTAGE
FTNVD	29	51.8%
LSCS	27	48.2%
TOTAL	56	100%

Out of 56 women who developed preeclampsia,51% delivered by vaginal delivery and 48% delivered by LSCS which is not statistically significant

TABLE XVII

Crosstab

			ALPHA1_GROUP		Total
			0-1.86	ABOVE 1.86	
MODE OF DELIVERY	FTNVD	Count	32	30	62
		% within ALPHA1_GROUP	74.4%	52.6%	62.0%
	LSCS	Count	11	27	38
		% within ALPHA1_GROUP	25.6%	47.4%	38.0%
Total		Count	43	57	100
		% within ALPHA1_GROUP	100.0%	100.0%	100.0%

Pearson Chi-Square=4.938* p=0.026

TABLE XVIII

Crosstab

			FETAL_GROUP		Total
			0-1.92	ABOVE 1.92	
MODE OF DELIVERY	FTNVD	Count	33	29	62
		% within FETAL_GROUP	75.0%	51.8%	62.0%
	LSCS	Count	11	27	38
		% within FETAL_GROUP	25.0%	48.2%	38.0%
Total		Count	44	56	100
		% within FETAL_GROUP	100.0%	100.0%	100.0%

Pearson Chi-Square=5.636* p=0.018

There is no statistical significance between mode of delivery and values of fetal hemoglobin and alpha 1 microglobulin

TABLE XIX

Birth Weight Group	Frequency	Percent
<2.5 K.GMS	5	5.0
2.5-3.0 KGMS	57	57.0
ABOVE 3.0 KGMS	38	38.0
Total	100	100.0

FIGURE X

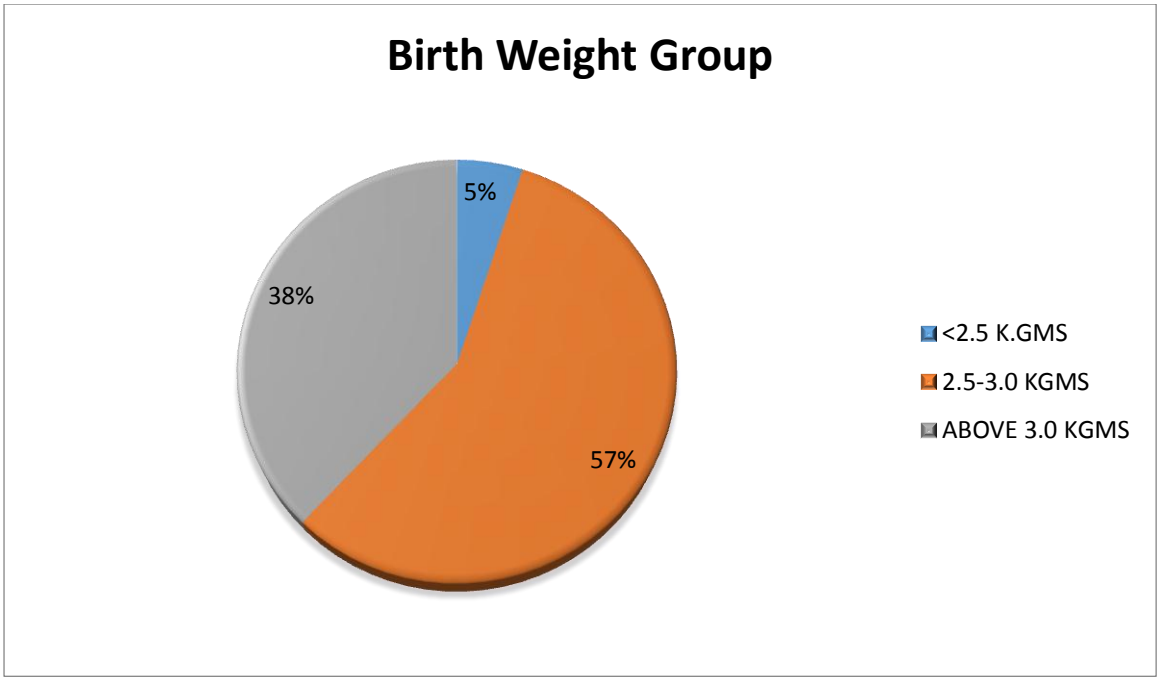


TABLE XX

Crosstab

			DEVELOPED PE		Total
			No	Yes	
birth weight group	<2.5 K.GMS	Count	3	2	5
		% within DEVELOPED PE	6.8%	3.6%	5.0%
	2.5-3.0 KGMS	Count	21	36	57
		% within DEVELOPED PE	47.7%	64.3%	57.0%
	ABOVE 3.0 KGMS	Count	20	18	38
		% within DEVELOPED PE	45.5%	32.1%	38.0%
Total		Count	44	56	100
		% within DEVELOPED PE	100.0%	100.0%	100.0%

Pearson Chi-Square=2.854 p=0.240

Birth weight of majority of babies (57%) were between 2.5 to 3.0 kgs.38% of babies were above 3.0 kgs and 5% of babies were less than 2.5 kgs.

TABLE XXI

Crosstab

			ALPHA1_GROUP		Total
			0-1.86	ABOVE 1.86	
birth weight group	<2.5 K.GMS	Count	3	2	5
		% within ALPHA1_GROUP	7.0%	3.5%	5.0%
	2.5-3.0 KGMS	Count	21	36	57
		% within ALPHA1_GROUP	48.8%	63.2%	57.0%
	ABOVE 3.0 KGMS	Count	19	19	38
		% within ALPHA1_GROUP	44.2%	33.3%	38.0%
Total		Count	43	57	100
		% within ALPHA1_GROUP	100.0%	100.0%	100.0%

Pearson Chi-Square=2.231 p=0.328

TABLE XXII

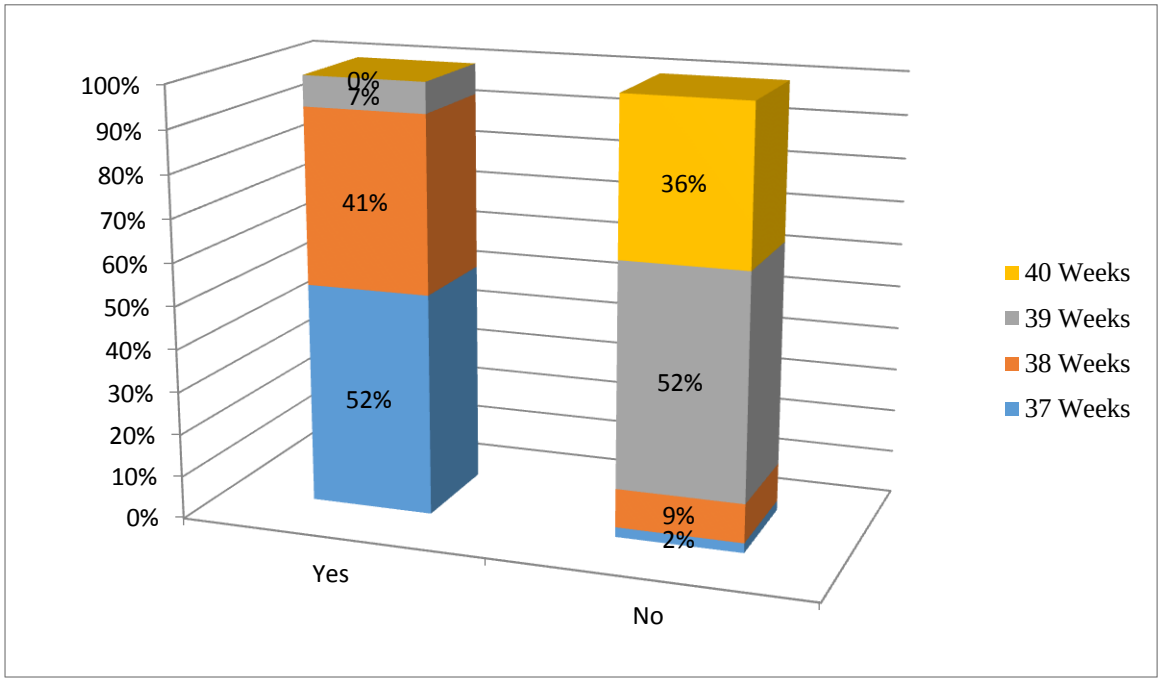
Crosstab

			FETAL_GROUP		Total
			0-1.92	ABOVE 1.92	
birth weight group	<2.5 K.GMS	Count	3	2	5
		% within FETAL_GROUP	6.8%	3.6%	5.0%
	2.5-3.0 KGMS	Count	21	36	57
		% within FETAL_GROUP	47.7%	64.3%	57.0%
	ABOVE 3.0 KGMS	Count	20	18	38
		% within FETAL_GROUP	45.5%	32.1%	38.0%
Total		Count	44	56	100
		% within FETAL_GROUP	100.0%	100.0%	100.0%

Pearson Chi-Square=2.854 p=0.240

There is no statistical significance between birth weight of babies and values of fetal hemoglobin and alpha 1 microglobulin

FIGURE XI: GESTATIONAL AGE OF DELIVERY



Most of the women who developed preeclampsia delivered around 37 weeks. This is due to the higher induction rate in these women

FIGURE XII

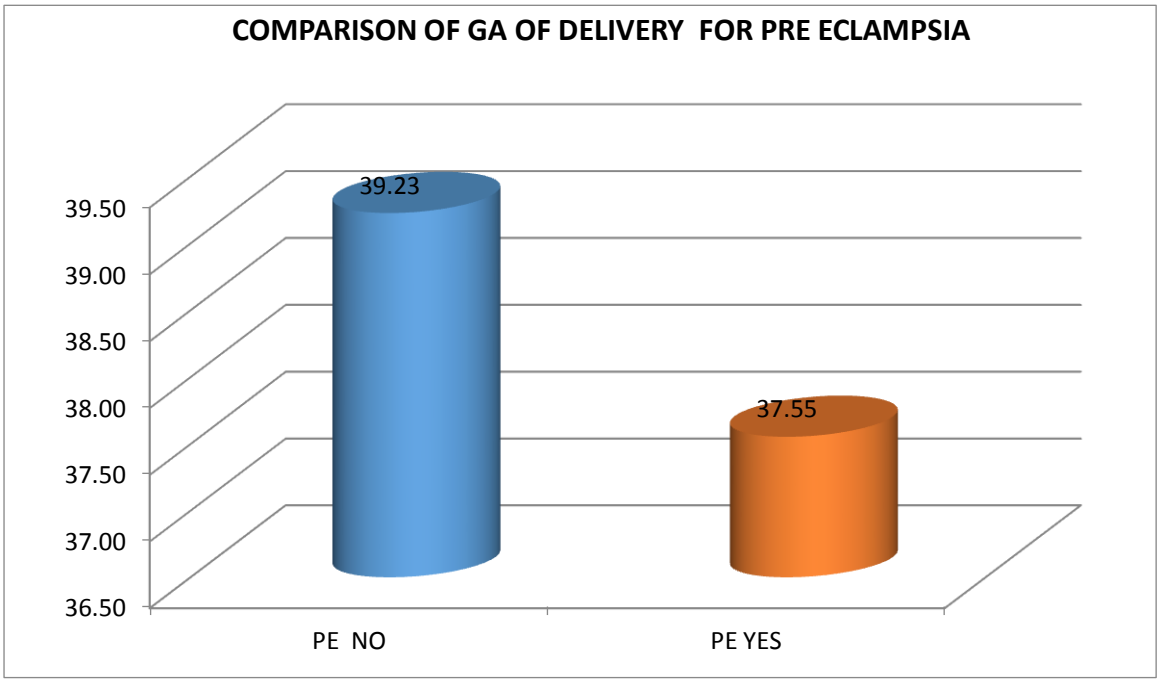


TABLE XXIII

GA_OF_DELIVERY * DEVELOPED_PE Crosstabulation

			DEVELOPED_PE		Total
			No	Yes	
GA_OF DELIVERY	37.00	Count	1	29	30
		% within DEVELOPED_PE	2.3%	51.8%	30.0%
	38.00	Count	4	23	27
		% within DEVELOPED_PE	9.1%	41.1%	27.0%
	39.00	Count	23	4	27
		% within DEVELOPED_PE	52.3%	7.1%	27.0%
	40.00	Count	16	0	16
		% within DEVELOPED_PE	36.4%	0.0%	16.0%
Total		Count	44	56	100
		% within DEVELOPED_PE	100.0%	100.0%	100.0%

Pearson Chi-Square=68.419** P<0.001

51.8% of women who developed preeclampsia delivered around 37 weeks of gestation which is statistically significant

COMPARISON OF INTERVAL SCALING VARIABLES LIKE AGE, BMI, WEEKS OF GA, FETAL, ALPHA1, GA OF DELIVERY, BIRTH WEIGHT (TABLE XX1V)

Independent Samples Test

DEVELOPED PE		N	Mean	Std. Deviation	Std. Error Mean	T VALUE	P VALUE
AGE	No	44	26.227	2.208	0.333	0.231	0.818
	Yes	56	26.339	2.546	0.340		
BMI	No	44	21.215	3.343	0.504	1.437	0.154
	Yes	56	22.593	5.629	0.752		
WEEKS OF GA	No	44	12.977	1.320	0.199	0.171	0.865
	Yes	56	13.018	1.053	0.141		
ALPHA 1 MICROGLOBULIN	No	44	1.490	0.183	0.028	17.788**	P<0.001
	Yes	56	2.446	0.317	0.042		
FETAL HEMOGLOBIN	No	44	0.994	0.489	0.074	22.928**	P<0.001
	Yes	56	3.219	0.476	0.064		
GA OF DELIVERY	No	44	39.227	0.711	0.107	12.460**	P<0.001
	Yes	56	37.554	0.630	0.084		
BIRTH WEIGHT	No	44	2.950	0.280	0.042	1.301	0.196
	Yes	56	2.882	0.241	0.032		

**P<0.001

DESCRIPTIVE FOR INTERVAL SCALING (TABLE XXV)

	Statistic						
		95% Confidence Interval for Mean					
	Mean	Lower Bound	Upper Bound	Median	Std. Deviation	Minimum	Maximum
Age	26.290	25.815	26.765	26.000	2.392	22.00	32.00
BMI	21.987	21.036	22.937	21.295	4.789	12.90	45.81
Weeks of GA	13.000	12.767	13.233	13.000	1.172	11.00	16.00
Alpha 1 microglobulin	2.025	1.917	2.133	2.095	0.546	1.04	3.20
Fetal hemoglobin	2.240	2.000	2.480	2.580	1.209	.28	3.66
GA of delivery	38.290	38.078	38.502	38.000	1.066	37.00	40.00
Birth weight	2.912	2.860	2.964	2.900	0.260	2.40	3.50

The mean age of the women in the study was 26.22. The mean age of women who developed preeclampsia was 26.3±2.2 years.

Mean BMI of women who developed preeclampsia was 22.5±5.6. Mean BMI of normal pregnant women was 21.2±3.3.

And mean gestational age of delivery was 37.5±0.6 weeks.

FIGURE XIII

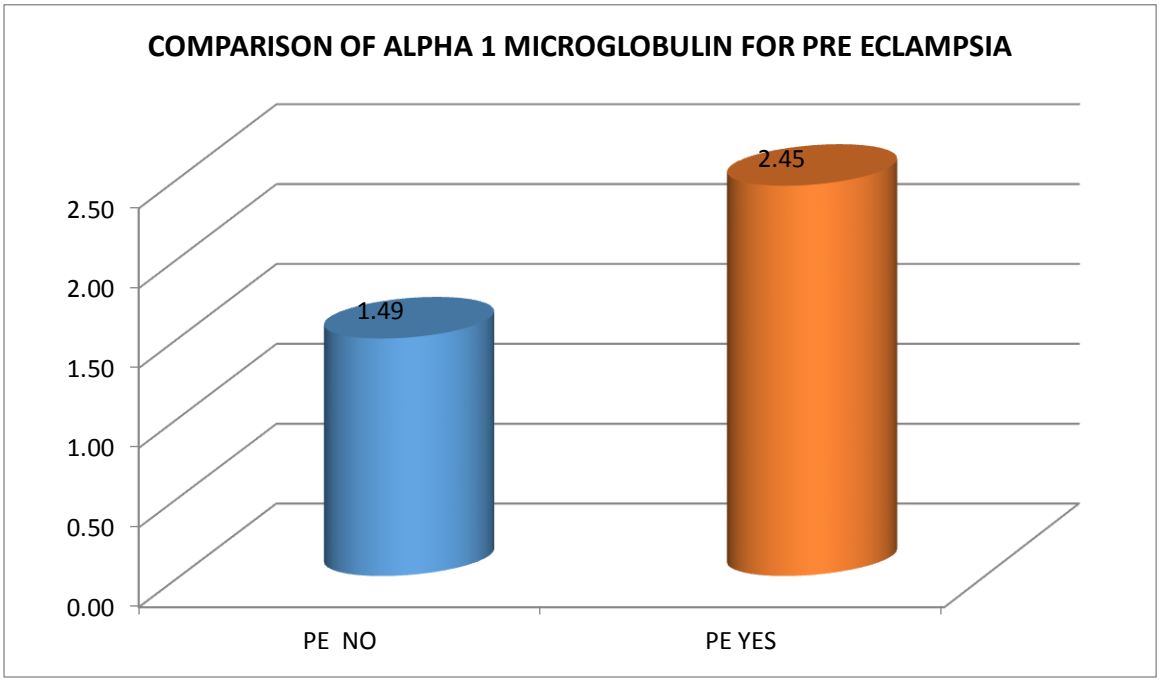


TABLE XXVI

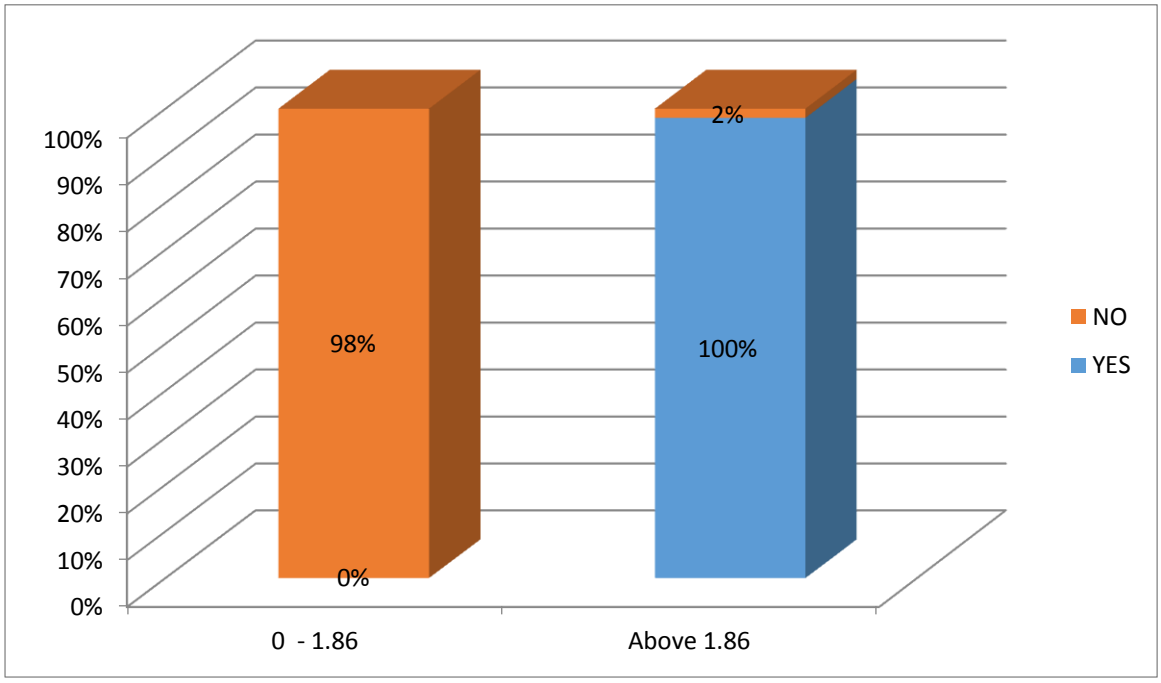
Crosstab

			DEVELOPED PE		Total
			No	Yes	
ALPHA 1 GROUP	0-1.86	Count	43	0	43
		% within DEVELOPED PE	97.7%	0.0%	43.0%
	ABOVE 1.86	Count	1	56	57
		% within DEVELOPED PE	2.3%	100.0%	57.0%
Total		Count	44	56	100
		% within DEVELOPED PE	100.0%	100.0%	100.0%

Pearson Chi-Square=96.013** P<0.0001

There exists a statistical significance between the high levels of alpha 1 microglobulin and development of preeclampsia

FIGURE XIV



Sensitivity of alpha 1 microglobulin is 100% and specificity is 23%

FIGURE XV

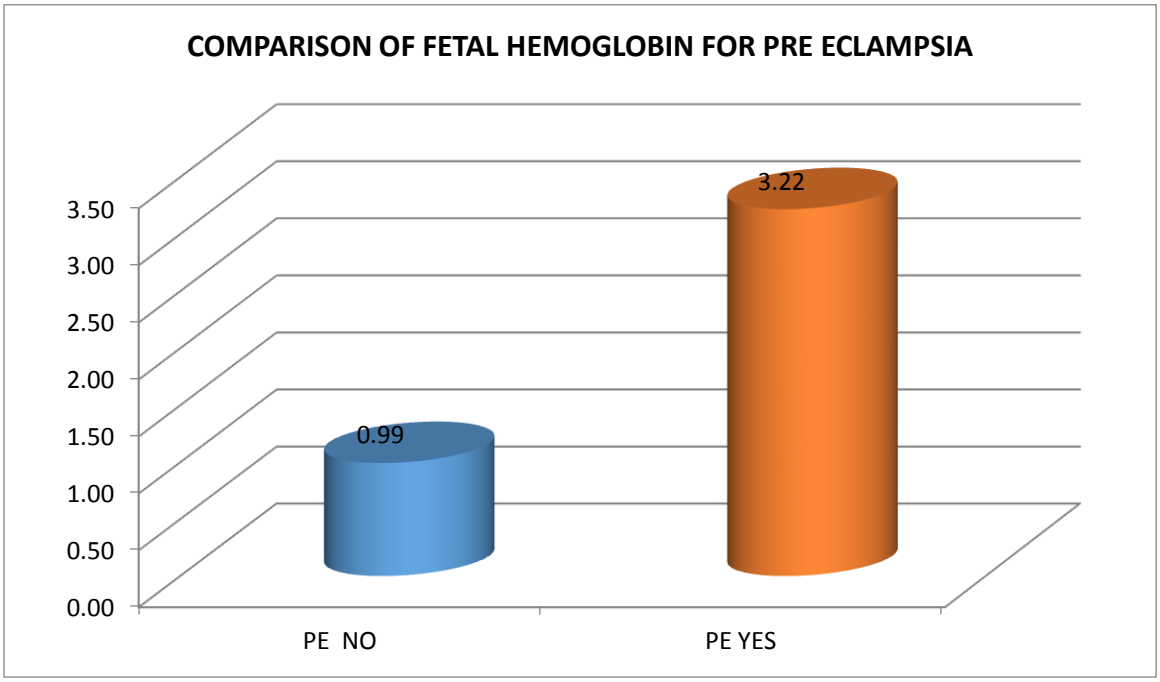


TABLE XXVII

			DEVELOPED PE		Total
			No	Yes	
FETAL GROUP	0-1.92	Count	43	1	44
		% within DEVELOPED PE	97.7%	1.8%	44.0%
	ABOVE 1.92	Count	1	55	56
		% within DEVELOPED PE	2.3%	98.2%	56.0%
Total		Count	44	56	100
		% within DEVELOPED PE	100.0%	100.0%	100.0%

Pearson Chi-Square=92.048** P<0.0001

Sensitivity of fetal hemoglobin is 98.2% and specificity is 23%

TABLE XXVIII

ALPHA2_GROUP * FETAL_GROUP Cross Tabulation

			FETAL_GROUP		Total
			0-1.92	ABOVE 1.92	
ALPHA1 GROUP	0-1.86	Count	42	1	43
		% within FETAL_GROUP	95.5%	1.8%	43.0%
	ABOVE 1.86	Count	2	55	57
		% within FETAL_GROUP	4.5%	98.2%	57.0%
Total		Count	44	56	100
		% within FETAL_GROUP	100.0%	100.0%	100.0%

Mcnemar p>0.05 so sensitivity was difference between two test

TO FIND OUT THE CUTOFF VALUES FOR ALPHA 1 AND FETAL HB WE USED ROC CURVE

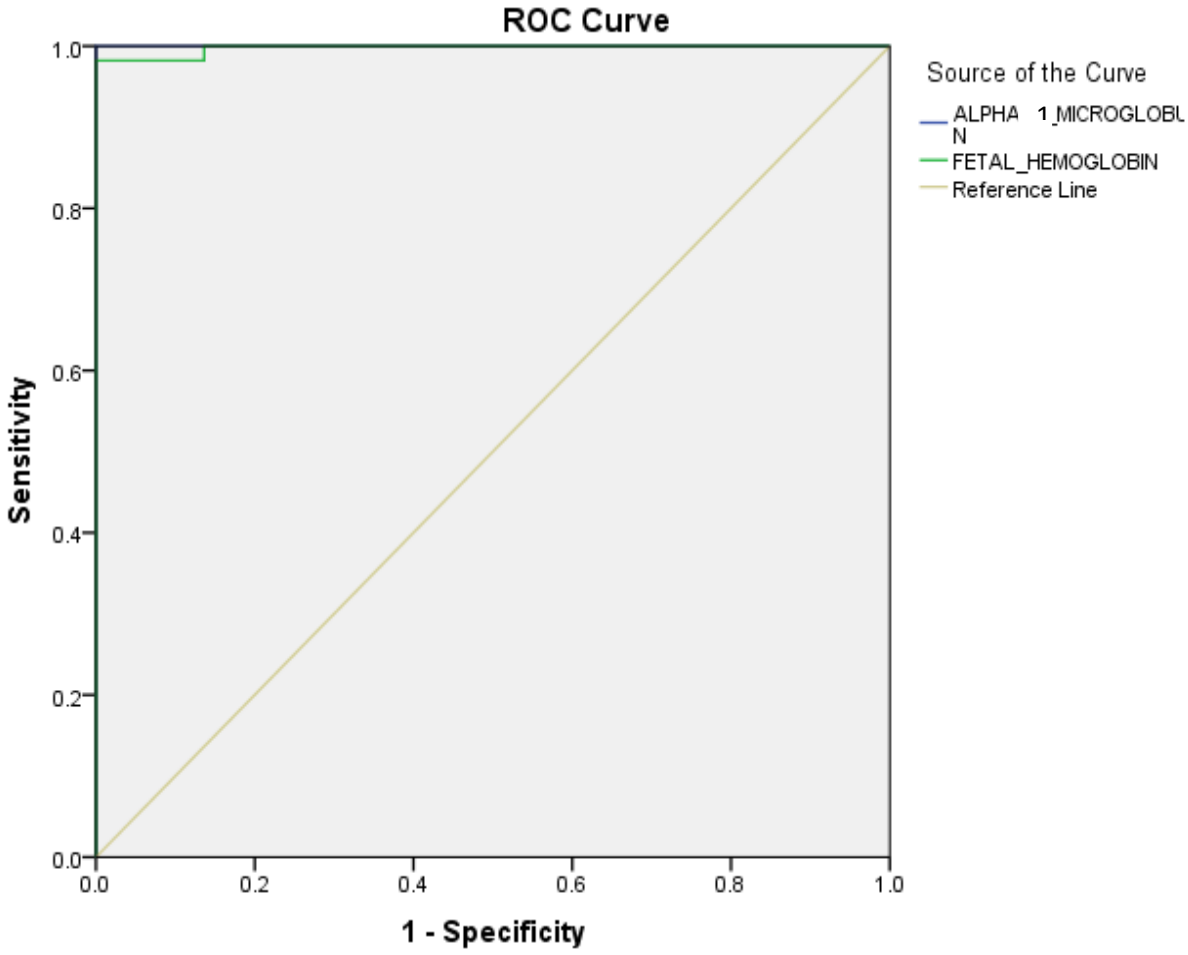


TABLE XXIX

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
ALPHA 1 MICROGLOBULIN	1.000	.000	.000	1.000	1.000
FETALHEMOGLOBIN	.998	.003	.000	.992	1.000

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Coordinates of the Curve			
Test Result Variable(s)	**Positive if Greater Than or Equal To[a]**	**Sensitivity**	**1 - Specificity**
ALPHA_1 MICROGLOBULIN	.0400	1.000	1.000
	1.1250	1.000	.977
	1.2300	1.000	.955
	1.2850	1.000	.932
	1.3250	1.000	.886
	1.3350	1.000	.818
	1.3500	1.000	.705
	1.3650	1.000	.682
	1.3850	1.000	.659
	1.4050	1.000	.614
	1.4150	1.000	.591
	1.4250	1.000	.568
	1.4350	1.000	.500
	1.4800	1.000	.477
	1.5250	1.000	.409
	1.5450	1.000	.386
	1.5850	1.000	.295
	1.6200	1.000	.250
	1.6350	1.000	.227
	1.6450	1.000	.205
	1.6800	1.000	.182
	1.7150	1.000	.159
	1.7250	1.000	.136
	1.7305	1.000	.114
	1.7505	1.000	.091
	1.7750	1.000	.068
	1.8600	1.000	.023
FETAL_HEMOGLOBIN	-.7200	1.000	1.000
	.3100	1.000	.977
	.3550	1.000	.955
	.3750	1.000	.932
	.4050	1.000	.909
	.4400	1.000	.886
	.4800	1.000	.864
	.5200	1.000	.818
	.5700	1.000	.773
	.6250	1.000	.750
	.6450	1.000	.727
	.6650	1.000	.705

	.7250	1.000	.682
	.7750	1.000	.659
	.7850	1.000	.614
	.8100	1.000	.591
	.8400	1.000	.568
	.8600	1.000	.523
	.8750	1.000	.477
	.8805	1.000	.455
	.9155	1.000	.432
	.9600	1.000	.409
	.9750	1.000	.386
	1.1500	1.000	.318
	1.3350	1.000	.273
	1.4400	1.000	.250
	1.5450	1.000	.205
	1.5700	1.000	.182
	1.6150	1.000	.159
	1.6650	1.000	.136
	1.7300	.982	.136
	1.7850	.982	.091
	1.8000	.982	.068
	1.8300	.982	.045
	1.9150	.982	.023

TABLE XXX

Coordinates of the Curve			
Test Result Variable(s)	**Positive if Greater Than or Equal To[a]**	**Sensitivity**	**1 - Specificity**
ALPHA 1 GROUP	1.8600	1.000	.023
FETAL HEMOGLOBIN	1.9150	.982	.023

The cutoff value for alpha 1 microglobulin is 1.86 above which most of the pregnant women developed preeclampsia.

The cut off value of fetal hemoglobin is 1.92 above which most of the pregnant women developed preeclampsia.

TABLE XXXI

ALPHA2GROUP * FETAL GROUP Cross tabulation

			FETAL GROUP		Total
			0-1.92	ABOVE 1.92	
ALPHA 1 GROUP	0-1.86	Count	42	1	43
		% within FETALGROUP	95.5%	1.8%	43.0%
	ABOVE 1.86	Count	2	55	57
		% within FETALGROUP	4.5%	98.2%	57.0%
Total		Count	44	56	100
		% within FETALGROUP	100.0%	100.0%	100.0%

Pearson Chi-Square=88.204** P<0.001

SENSTIVITY	95.45%
SPECIFICITY	98.21%
POSTIVE PREDICTIVE VALUE	97.67%
NEGATIVE PREDICTIVE VALUE	96.49%
DISEASE PREVALENCE	44.00%
DIAGNOSTIC ACCURACY	97
FALSE POSITIVITY RATE	1.79%
FALSE NEGATIVITY RATE	4.55%
POSTIVE LR	53.45
NEGATIVE LR	0.05

DISCUSSION

This is a prospective cohort study to establish association between high levels of fetal hemoglobin and alpha 1 microglobulin in pregnant women of 10 to 16 weeks of GA and subsequent development of preeclampsia. The study was conducted in the Department of Obstetrics and Gynaecology, ISO, KGH, Triplicane from September 2016 to August 2017.

There are only few studies in literature regarding the association between high levels of fetal hemoglobin and alpha 1 microglobulin and development of preeclampsia. We included 100 pregnant women of GA 10 TO 16 weeks without any comorbidities.

BASELINE CHARACTERISTICS

The mean age of the women with preeclampsia in the present study was 26.22 and it was similar to the studies reported in literature.

Preeclampsia is more common in primigravida and its incidence decreases in future pregnancies due to loss of maternal tolerance to paternally derived placental and fetal antigens.

Moore et al(6) in his study found 71% of women as primigravida. In luealonet al(8)study 64.1% were primigravida. In our study 53.6% were primigravida. In a study on biomarkers for preeclampsia by kusanovic et al(7) 61.3% were primigravida.

The mean BMI of women who developed preeclampsia in our study was 21.74with a range of 18.5 to 24.99. In a study by Anderson et al(1) BMI of women who developed preeclampsia was 26.9. This difference is due to different ethnicity, race, socioeconomic status, eating habits etc

In our study the mean arterial pressure at admission was 111.33 mm of Hg for preeclamptic women and 88.33 mm of Hg in normotensive women.

All women in the study required one or more antihypertensives for control of blood pressure in the antenatal period. Tuffnell et al (11)used antihypertensives medication in 53% of women with preeclampsia.In the study by Podynow et al(2),43% of women required antihypertensives medication in the antenatal period. The difference in the requirements of antihypertensives in the antenatal period may be because all groups of hypertensive disorders were included in all the studies.

The induction rate was higher in women who developed preeclampsia compared to women who did not develop preeclampsia. Out of 56 women who had developed preeclampsia, labour was induced in 41, spontaneous onset of labour in 3 women and 12 underwent elective caesarean section..In the study by Lisa et al caesarean delivery was significantly more in preeclamptic women. However in our study there

was no significant difference between caesarean section and vaginal delivery

Mean gestational age at delivery in our study was 37 weeks. Anderson et al(1) observed in his study the mean gestational age was 36.7 weeks. Luealon et al (8) studied risk factors of preeclampsia and found that the mean gestational age at delivery as 36.5±3.1 weeks. Joanne et al observed the gestational age at delivery in preeclamptic women as 35 weeks. This was due to the fact that all preeclamptic women were induced at 37 weeks.

In our study mean birth weight of preeclamptic women was 2.75 kg. This is in accordance to the study by Anderson et al(1), where the mean birth weight of preeclamptic women was 2.716 kg.

In our study 51% delivered vaginally. However there is no statistical significance between mode of delivery and preeclampsia. Study by Anderson et al (1)showed a mean value of α1 microglobulin of 1.95ng/ml as cutoff for predicting preeclampsia. My study also supports the fact. The cutoff value of α1 microglobulin in my study was 1.86ng/ml after applying ROC curve. Sensitivity of α1 microglobulin is 100% and specificity is 25%.

Out of the 56 women who developed preeclampsia 51% delivered by vaginal delivery and 49% by LSCS. But this was not statistically significant.

Similar study by Anderson et al(1) showed a mean value of fetal hemoglobin as 1.38ng/ml as cutoff for predicting preeclampsia. In my study, cut off value for fetal hemoglobin for predicting preeclampsia was 1.91ng/ml. Sensitivity of fetal hemoglobin is 98.2% and specificity is 23%.

The combined sensitivity is 95.45% and specificity of both the tests is 98.21%. In a study by Anderson et al (1) combined sensitivity is 90% at 30% screen positivity rate.

Our data indicate the combination of HbF and α1 microglobulin levels may be used as first trimester biomarker for screening preeclampsia. The predictive values obtained in combination compare favourably with other preeclampsia biomarkers.

LIMITATIONS

- Small study population
- Important variables like race, ethnicity were not studied
- Severity of preeclampsia not determined
- Comparison of levels of fetal hemoglobin and alpha 1 microglobulin with other biochemical markers of preeclampsia like VEGF were not studied

SUMMARY

This prospective cohort study was conducted in the Department of Obstetrics and Gynaecology, ISO,KGH, Triplicane, Chennai. One hundred women were enrolled in the study. Plasma levels of HbF and α1 microglobulin were estimated.

Findings are summarized as follows:

- Mean age of women who developed preeclampsia was 26.22.
- Majority of women were primigravida.
- Mean BMI of preeclamptic women was 21.74.
- Mean arterial pressure was 111.33 mm of Hg in women who developed preeclampsia and 88.33 mm of Hg in normal pregnant women.
- Majority of the women who developed preeclampsia required one or more antihypertensives for control of blood pressure in the antenatal period.
- Induction of preeclamptic women were done at 37 weeks
- Mean gestational age at delivery was 37 weeks.
- Vaginal delivery was slightly higher in preeclamptic women. But this was not statistically significant.

- Mean birth weight of babies born to preeclamptic mother was 2.75kg.
- Serum levels of fetal hemoglobin and α1 microglobulin were higher in preeclamptic women compared with normal women. The difference was statistically significant.

CONCLUSION

From the present study it may be concluded that

Higher values of HbF and α1 microglobulin in pregnant women between 10 to 16 weeks gestational age positively correlates with development of preeclampsia in those women.

HbF and α1 microglobulin can be used as biomarkers in late first trimester and early second trimester of pregnancy for detecting preeclampsia.

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PROFORMA

- NAME
- AGE
- IP NO
- PARITY
- ADDRESS
- PREVIOUS OBSTETRIC HISTORY
- LMP/EDD
- GESTATIONAL AGE
- BMI
- MARITAL H/O
- PAST H/O
- HIGH RISKS DURING PREGNANCY AND DELIVERY
- EXAMINATION AT ADMISSION

  Pallor

  Oedema

  Pulse rate

  Respiratory rate

  Systolic Blood pressure

  Diastolic blood pressure

- **ANTIHYPERTENSIVE DRUGS**

  Name of the drug

  Dosage

  Since which GA

- CVS Examination
- RS Examination
- **INVESTIGATIONS**

  Complete blood count

  Liver function tests

  Renal function tests

  Urine protein

  24 hour urine protein

  Fundus examination

- **BABY DETAILS**

- Mode of delivery
- Sex of baby
- Birth weight
- APGAR
- Mother side/ admitted

INFORMATION SHEET

- We are conducting a study of levels of fetal hemoglobin and alpha 1 microglobulin in pregnant women and their association with the development of preeclampsia. Your participation in the study is very valuable to us.

- The purpose of this study is to find out whether fetal hemoglobin and alpha 1 microglobulin can be used as biochemical markers for predicting preeclampsia in pregnant women

- We will do fetal hemoglobin and alpha 1 microglobulin assay in all pregnant women

- The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

- Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

- The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of investigator Signature of participant

தகவல் தாள்

- கர்ப்பிணிப் பெண்களின் இரத்தத்தில் உள்ள ஃபீட்டல் ஹீமோகுளோபின் மற்றும் ஆல்ஃபா 1 மைக்ரோகுளோபினின் அளவை நாம் ஆய்வு செய்து வருகிறோம். ஆய்வில் உங்கள் பங்களிப்பு எங்களுக்கு மிகவும் மதிப்புமிக்கதாகும்.

- இந்த ஆய்வின் நோக்கம், கர்ப்பிணி பெண்களுக்கு கர்ப்ப காலத்தில் ஏற்படும் இரத்த கொதிப்பை கணிப்பதற்கான உயிர்வேதியியல் குறிப்பான்களாக ஃபீட்டல் ஹீமோகுளோபின் மற்றும் ஆல்பா 1 மைக்ரோகுளோபினின்களைப் பயன்படுத்தலாமா என்பது கண்டுபிடிக்கவே

- நாங்கள் கர்ப்பிணிப் பெண்களில் பீட்டல் ஹீமோகுளோபின் மற்றும் ஆல்ஃபா 1 மைக்ரோகுளோபலின் மதிப்பீடு செய்வோம்

- ஆய்வில் உள்ள நோயாளிகளின் தனியுரிமை ஆய்வு முழுவதும் பராமரிக்கப்படும். ஆராய்ச்சியின் விளைவாக எந்தவொரு வெளியீடும் ஏற்பட்டால், தனிப்பட்ட நபரின் அடையாளம் வெளியிடப்படாது.

- இந்த ஆய்வில் பங்கு பெறுவது தனிநபரின் விருப்பமாக உள்ளது. இந்த ஆய்வில் பங்கேற்க வேண்டுமா அல்லது எப்போது வேண்டுமானாலும் விலகலாமா என்பதைத் தீர்மானிக்க நீங்கள் சுதந்திரமாக இருக்கின்றீர்கள்.

- ஆய்வின் முடிவுகளின் முடிவில் அல்லது சிறப்புப் பரீட்சையின் பெறுபேறுகள் உங்களை ஆய்வுக்கு உட்படுத்தியிருக்கலாம் அல்லது ஆய்வு அல்லது சிகிச்சையில் உதவுவதற்கு ஏதேனும் அசாதாரணமானவை எனக் கண்டறிந்து இருக்கலாம்.

புலன்விசாரணியின் கையொப்பம் பங்கேற்பாளரின் கையொப்பம்

INFORMED CONSENT FORM

Title: Fetal hemoglobin and alpha 1 microglobulin as biochemical markers in predicting preeclampsia in late first trimester and early second trimester of pregnancy

Name of the investigator: Dr. I. INBA PRIYANKA

Name of the participant:

Name of the institution: Institute of obstetrics and gynaecology, MMC, Chennai.

I _____ have read the information in this form(or it has been read to me).I was free to ask any questions and they have been answered. I am over 18 years of age and exercising my power of choice, hereby give my consent to be included as a participant in this study.

1. I have read and understood this consent form and the information provided to me.

2. I have read the consent document explained to me.

3. I have been explained about the nature of the study.

4. I have been explained my rights and responsibilities by the invigilator,

5. I have informed the investigator of all the treatments I am taking or have taken in the past months/years including any native treatments

6. I have been advised about the risks associated with my participation in the study

7. I agree to cooperate with the investigator and I will inform him/her immediately if I suffer unusual symptoms.

8. I have not participated in any research study within the past.

9.I am aware of the fact that I can opt out of the study at any time without having to give any reason. This will not affect my future treatment in the hospital.

10. I am also aware that the investigators may terminate my participation in this study at any time, for any reason, without my consent.

11. I hereby give permission to the investigators to release the information obtained from me as result of participation in this study to the sponsors, regularity authorities, Govt. agency and IEC if required.

12. I understand that my identity will be kept confidential if my data are publicly presented.

13. I have had my questions answered to my satisfaction.

14. I consent voluntarily to participate in the research/study

I am aware that if I have any question during this study, I should contact the investigator. By signing this consent form, I attest that the information given in this document has been clearly explained to me and understood by me. I will be given a copy of this consent document.

FOR ADULT PARTICIPANTS

1. Name and signature /thumb impression of the participant(or legal representative if participant incompetent)
   Name_____ Signature_____ Date_____

2. Name and signature of impartial witness(required for illiterate patients)
   Name_____ Signature _____Date_____

3. Name and signature of the investigator or his representative obtaining consent
   Name_____ Signature_____ Date_____

தகவல் தொடர்பு படிவம்

தலைப்பு: 10-16 **வாரங்களில், கணிக்கும் உயிர்வேதியியல் குறிப்பான்கள் என ஃபீட்டல் ஹீமோகுளோபின் மற்றும் ஆல்பா** 1 **மைக்ரோகுளோபினின்**

புலன்விசாரணியின் பெயர்: டாக்டர். இ.இன்ப பிரியங்கா

பங்கேற்பாளரின் பெயர்:

நிறுவனத்தின் பெயர்: மகப்பேறியல் மற்றும் பெண்ணோயியல் நிறுவனம், எம்.எம்.சி, சென்னை.

நான் _____ இந்த படிவத்தில் தகவலைப் படித்திருக்கிறேன் (அல்லது அது எனக்குப் படிக்கப் பட்டுள்ளது). நான் எந்த கேள்விகளையும் கேட்க தயங்கவில்லை, அவை அனைத்திற்கும் பதில் கிடைத்தது. நான் 18 **வயதிற்கு மேல் இருக்கிறேன், தேர்வு செய்ய என் ஆற்றலைப் பயன்படுத்துகிறேன், இந்த ஆய்வில் பங்கேற்பாளராக சேர்க்கப்பட என் அனுமதியினை அளிக்கிறேன்.**

1. **இந்த ஒப்புதல் படிவத்தையும் எனக்கு வழங்கப்பட்ட தகவலையும் நான் வாசித்து புரிந்து கொண்டேன்.**

2. **ஒப்புதல் ஆவணத்தை நான் படித்திருக்கிறேன்.**

3. **ஆய்வின் தன்மை பற்றி நான் விளக்கப்பட்டுள்ளேன்.**

4. **எனது உரிமைகள் மற்றும் பொறுப்புகள் பற்றி நான் விளக்கப்பட்டுள்ளேன்.**

5. **கடந்த சில மாதங்களில் நான் எடுக்கும் அனைத்து சிகிச்சைகளுக்கும் புலன்விசாரணை அறிவித்திருக்கிறேன்**

6. **ஆய்வில் என் பங்களிப்புடன் தொடர்புடைய அபாயங்கள் பற்றி நான் அறிவுறுத்தப்பட்டிருக்கிறேன்**

7. **நான் புலனாய்வாளருடன் ஒத்துழைக்க ஒத்துக்கொள்கிறேன் மற்றும் நான் அசாதாரண அறிகுறிகளை அனுபவித்தால் உடனடியாக அவரை / அவளுக்கு தெரிவிப்பேன்.**

8. **கடந்த காலத்திற்குள் நான் எந்த ஆராய்ச்சியிலும் பங்கேற்கவில்லை.**

9. **எந்த நேரத்திலும் எந்தவொரு காரணத்திற்காகவும் நான் இந்த ஆய்வில் இருந்து விலகிக் கொள்ள முடியும் என்பதை நான் அறிந்திருக்கிறேன். இது என் எதிர்கால சிகிச்சையை மருத்துவமனையில் பாதிக்காது என்பதையும் அறிந்திருக்கிறேன்.**

10. **எந்தவொரு காரணத்திற்காகவும், என் அனுமதியின்றி ஆய்வாளர் என் பங்கேற்பை நீக்க முடியும் என்பதை அறிந்திருக்கிறேன்.**

11. **இந்த ஆய்வில் பங்கேற்பாளர்களான, ஆய்வாளர்கள் அரசு நிறுவனம் மற்றும்** IEC **ஆகியவற்றிற்கு தேவைப்பட்டால், என்னிடமிருந்து பெறப்பட்ட தகவலை வெளியிட புலனாய்வுக்கு அனுமதி அளித்தேன்.**

12. **எனது தரவு பகிரங்கமாக வழங்கப்பட்டால், எனது அடையாளத்தை ரகசியமாக வைத்திருப்பதை நான் புரிந்துகொள்கிறேன்.**

13. **என் திருப்திக்கு என் கேள்விகளுக்கு பதில் அளிக்கப்பட்டது.**

14. **ஆராய்ச்சி / ஆய்வுகளில் பங்கேற்க நான் தன்னார்வத்துடன் ஒப்புக்கொள்கிறேன்**

இந்த ஆய்வின் போது எனக்கு ஏதாவது கேள்விகள் இருந்தால், நான் புலனாய்வாளரை தொடர்பு கொள்ள வேண்டும் என்று எனக்கு தெரியும். இந்த ஒப்புதலுக்கான படிவத்தை கையொப்பமிடுவதன் மூலம், இந்த ஆவணத்தில் கொடுக்கப்பட்ட தகவல்கள் தெளிவாக எனக்கு விளக்கப்பட்டு எனக்கு புரிந்துவிட்டது என்பதை நான் சான்றளிக்கிறேன். இந்த ஒப்புதல் ஆவணத்தின் நகலை எனக்கு வழங்கப்படும்.

பழங்குடி வகுப்பாளர்களுக்கு

பங்கேற்பாளரின் பெயர் மற்றும் கையொப்பம் / கட்டைவிரல் உணர்வை (அல்லது பங்கேற்பாளர் தகுதியற்றவர் எனில் சட்ட பிரதிநிதி)

பெயர்_____ கையொப்பம் _____ தேதி _____

பாரபட்சமற்ற சாட்சியின் பெயர் மற்றும் கையொப்பம் (படிப்பறிவற்ற நோயாளிகளுக்கு தேவை)

பெயர்_____ கையொப்பம் _____DATE_____

புலன்விசாரணை அல்லது அவரது பிரதிநிதி அனுமதிப்பத்திரத்தின் பெயர் மற்றும் கையொப்பம்

பெயர்_____ கையொப்பம் _____ தேதி _____

MASTER CHART

MASTER CHART

SL NO	NAME	AGE	PARITY	HEIGHT	WEIGHT	BMI	WEEKS OF GA	ALPHA 1 MICRO GLOBULIN	FETAL HEMO GLOBIN	DEVELOPED PE	MODE OF DELIVERY	GA OF DELIVERY	BIRTH WEIGHT
1	ROJA	24	MULTI	161	65	25.07	12	1.731	0.28	NO	FTNVD	38	3.1
2	RANI	23	PRIMI	158	38	15.22	13	2.022	3.63	YES	LSCS	39	2.8
3	KOKILA	22	MULTI	157	52	21.09	12	1.56	0.34	NO	FTNVD	37	3.5
4	DEVI	24	PRIMI	157	80	32.45	13	2.52	2.3	YES	LSCS	39	3.1
5	LAVANYA	23	MULTI	146	45	21.11	14	1.25	0.51	NO	FTNVD	38	3.2
6	SALAMMAL	25	PRIMI	146	40	18.76	13	2.88	1.68	YES	LSCS	39	2.7
7	DIVYA	31	PRIMI	162	62	23.62	15	1.4	0.61	NO	FTNVD	38	3.4
8	ASHWINI	26	MULTI	163	84	31.61	14	2.27	2.99	YES	LSCS	37	3.2
9	GEETHA	27	PRIMI	155	80	33.29	13	2.16	3.65	YES	FTNVD	38	2.7
10	KAVITHA	30	PRIMI	151	43	18.85	12	1.94	0.881	NO	FTNVD	38	3.1
11	SASIREKHA	32	PRIMI	154	58	24.45	13	2.38	2.58	YES	LSCS	38	3.1
12	NADHIYA	27	MULTI	159	35	13.84	14	2.68	3.65	YES	FTNVD	37	3
13	SUGANYA	24	MULTI	155	31	12.9	15	1.34	0.64	NO	FTNVD	39	2.9
14	PONNI	28	PRIMI	152	46	19.9	14	2.21	3.01	YES	LSCS	38	2.6
15	BANUPRIYA	24	PRIMI	164	61	22.68	13	1.52	0.53	NO	FTNVD	39	3.2
16	SANGEETHA	25	PRIMI	154	40	16.86	14	2.19	3.64	YES	FTNVD	38	2.7
17	KAVITHA	31	PRIMI	152	36	15.58	12	2.62	2.89	YES	LSCS	38	3.2
18	MAHESHWARI	29	PRIMI	156	52	21.36	13	1.41	0.43	NO	FTNVD	39	3.1
19	VANI	28	MULTI	162	49	18.67	14	2.23	3.57	YES	LSCS	37	2.9
20	LAKSHMI	25	PRIMI	153	52	22.21	15	1.34	0.45	NO	FTNVD	40	3.4
21	SANGEETHA	24	PRIMI	156	47	19.31	12	2.19	3.64	YES	LSCS	37	2.8
22	FATHIMA	27	PRIMI	156	70	28.76	14	3.2	3.57	YES	FTNVD	37	3.1
23	LAKSHMI	23	PRIMI	164	53	19.7	12	1.34	1.58	NO	FTNVD	39	3.3
24	SANGEETHA	25	PRIMI	156	46	18.9	13	2.6	3.15	YES	LSCS	38	2.6
25	MONISHA	26	PRIMI	158	37	14.82	12	1.52	0.68	NO	FTNVD	40	2.9
26	BANUPRIYA	31	MULTI	160	60	23.43	11	1.4	0.95	NO	FTNVD	40	3.1
27	PARVATHI	28	MULTI	150	45	20	11	2.38	3.6	YES	LSCS	37	2.7
28	PRIYA	24	PRIMI	151	50	21.92	13	2.62	3.15	YES	FTNVD	38	2.9
29	SUDHA	27	PRIMI	156	40	16.43	12	1.56	1.98	NO	LSCS	39	3
30	GEETHA	25	MULTI	158	52	20.83	12	3.2	2.58	YES	FTNVD	38	2.8
31	PREETHI	23	PRIMI	151	74	32.45	14	2.62	3.65	YES	LSCS	37	3.2

32	SANDHYA	26	MULTI	160	50	19.53	13	1.44	0.85	NO	FTNVD	40	2.8
33	MUNEERA	28	PRIMI	154	52	21.92	15	2.38	2.83	YES	FTNVD	38	2.7
34	RANI	24	MULTI	160	49	19.14	13	1.04	0.97	NO	LSCS	40	2.7
35	LAKSHMI	27	PRIMI	155	63	26.22	14	2.6	2.89	YES	FTNVD	38	2.8
36	AHALYA	28	MULTI	147	99	45.81	12	2.24	2.5	YES	LSCS	38	2.9
37	SARA	26	PRIMI	172	66	22.3	13	1.37	1.53	NO	FTNVD	40	3.1
38	MEERAMA	25	MULTI	160	52	20.31	12	1.78	1.35	NO	LSCS	39	2.6
39	KOTESHWARI	27	PRIMI	156	74	30.4	13	2.49	3.65	YES	FTNVD	38	3.1
40	JAYAPRIYA	25	PRIMI	152	54	23.37	13	1.52	0.98	NO	FTNVD	40	2.9
41	GEETHA	27	PRIMI	160	62	24.21	13	2.77	3.66	YES	LSCS	37	3.2
42	MOHANA	25	MULTI	158	60	24.03	12	2.83	2.78	YES	FTNVD	37	2.6
43	PRIYA	24	MULTI	160	70	27.34	12	3.2	3.18	YES	LSCS	37	3.2
44	VALARMATHY	27	PRIMI	158	53	21.23	11	1.61	1.78	NO	FTNVD	39	2.7
45	SAIRA	24	PRIMI	164	70	26.02	14	2.23	2.9	YES	LSCS	38	3.1
46	VASUKI	28	PRIMI	148	37	16.82	11	1.72	0.87	NO	FTNVD	39	3.2
47	RANI	29	MULTI	154	70	29.51	15	2.41	3.66	YES	FTNVD	38	2.7
48	SEVANTHI	26	MULTI	155	56	23.3	13	2.38	3.02	YES	LSCS	37	2.9
49	YASMIN	25	MULTI	143	48	23.47	16	1.33	1.81	NO	LSCS	39	2.6
50	JAYA	31	MULTI	150	52	23.11	12	2.49	3.61	YES	FTNVD	38	3.2
51	SELVI	25	PRIMI	154	35	14.75	13	1.63	0.77	NO	FTNVD	39	3.1
52	LAVANYA	32	PRIMI	156	40	16.43	14	2.15	2.81	YES	FTNVD	37	2.8
53	SUBHA	26	PRIMI	158	62	24.83	13	1.53	1.56	NO	LSCS	39	2.8
54	ARUNA	27	MULTI	160	62	24.21	12	2.6	3.65	YES	FTNVD	38	2.7
55	SANGEETHA	23	MULTI	158	31	14.81	12	2.31	2.38	YES	LSCS	38	2.9
56	MEERA	22	PRIMI	156	46	18.9	13	2.2	2.78	YES	FTNVD	39	2.6
57	KAVITHA	25	PRIMI	158	55	22.03	15	1.42	0.79	NO	LSCS	39	2.8
58	SHARMILA	24	MULTI	154	43	18.13	12	2.15	3.65	YES	FTNVD	38	2.4
59	KUMARI	28	MULTI	160	61	23.82	14	1.77	1.32	NO	LSCS	39	3.1
60	RUBY	26	PRIMI	158	56	22.43	12	1.65	0.53	NO	LSCS	40	2.9
61	RAJI	24	MULTI	162	52	19.81	13	2.38	3.61	YES	FTNVD	37	2.9
62	SAVITHRI	26	PRIMI	150	44	19.55	15	1.73	0.51	NO	FTNVD	39	3.4
63	JAYANTHI	29	MULTI	164	50	18.59	12	2.77	2.89	YES	FTNVD	37	2.8
64	SEETHA	26	PRIMI	150	52	23.11	13	1.56	0.38	NO	LSCS	40	3.2
65	MANI	25	PRIMI	156	44	18.08	14	3.2	3.5	YES	FTNVD	37	3.2
66	ESWARI	31	PRIMI	156	46	18.9	11	2.04	3.65	YES	FTNVD	37	2.9

67	ILAKIA	27	MULTI	150	50	22.22	11	1.43	0.98	NO	FTNVD	39	3.1
68	SWETHA	32	MULTI	162	48	18.29	13	2.15	3.55	YES	LSCS	37	3.4
69	VASUKI	25	MULTI	160	62	24.21	13	1.36	0.85	NO	FTNVD	40	3
70	PORKODI	24	MULTI	158	60	24.03	12	2.02	2.9	YES	FTNVD	37	3.4
71	JANAGI	28	PRIMI	148	55	25.11	11	2.38	3.18	YES	LSCS	38	2.7
72	RAJI	26	PRIMI	154	48	20.24	15	1.43	1.53	NO	FTNVD	39	2.6
73	NARKIS	25	PRIMI	160	49	19.14	13	2.62	3.66	YES	FTNVD	37	3.1
74	SUMATHY	27	PRIMI	154	52	21.92	14	2.38	3.65	YES	LSCS	37	2.6
75	JEYANTHI	24	MULTI	160	50	19.53	15	1.56	1.32	NO	FTNVD	40	2.8
76	BOMMI	31	MULTI	158	52	20.83	13	2.77	3.5	YES	FTNVD	38	2.5
77	VASANTHI	32	PRIMI	163	47	17.69	14	1.34	0.87	NO	FTNVD	39	2.7
78	THAMIZH	26	PRIMI	157	48	19.47	12	2.38	3.65	YES	FTNVD	38	2.6
79	KAVITHA	27	MULTI	160	52	20.31	13	2.15	2.78	YES	LSCS	37	2.8
80	SUSANA	26	MULTI	158	56	22.43	14	1.33	0.78	NO	FTNVD	40	2.6
81	MANI	25	PRIMI	160	54	21.09	15	2.04	3.52	YES	LSCS	37	2.8
82	KAVIYARASI	28	MULTI	164	51	18.96	12	1.32	1.65	NO	FTNVD	40	3.1
83	VENNILA	26	MULTI	154	70	29.51	14	2.02	2.78	YES	LSCS	38	2.7
84	RAJESHWARI	25	MULTI	155	52	21.64	15	2.38	3.66	YES	FTNVD	37	3.2
85	VIJAYA	28	PRIMI	156	48	19.72	13	1.61	0.37	NO	FTNVD	39	2.6
86	RANI	26	PRIMI	158	55	22.03	14	2.19	2.58	YES	LSCS	37	2.6
87	ARUNA	25	MULTI	160	61	23.82	12	1.43	1.78	NO	FTNVD	39	2.4
88	ANUPAMA	27	MULTI	158	56	22.43	13	2.63	3.65	YES	FTNVD	37	2.7
89	KALA	25	PRIMI	162	52	19.81	13	1.32	1.85	NO	FTNVD	40	2.5
90	SURIYA	27	PRIMI	151	65	28.5	14	1.71	0.83	NO	FTNVD	39	2.4
91	VASANTHA	24	MULTI	155	55	22.89	11	2.88	3.65	YES	LSCS	38	2.6
92	MALATHY	26	MULTI	160	62	24.21	12	1.34	1.79	NO	FTNVD	40	3.2
93	BHARATHY	23	PRIMI	158	60	24.03	13	2.15	2.83	YES	FTNVD	37	3.1
94	RITA	28	PRIMI	155	63	26.22	12	1.21	0.98	NO	FTNVD	39	2.8
95	INDIRA	25	PRIMI	160	49	19.14	13	2.38	3.65	YES	LSCS	37	2.9
96	SANGEETHA	24	MULTI	158	52	20.83	12	2.04	2.88	YES	FTNVD	37	3.2
97	UMA	29	MULTI	157	44	17.85	11	1.78	0.88	NO	LSCS	39	2.8
98	DURGA	25	MULTI	150	45	20	14	2.6	3.65	YES	FTNVD	37	2.8
99	ARCHANA	24	PRIMI	156	47	19.31	12	1.33	0.78	NO	LSCS	40	3.2
100	USHA	27	PRIMI	156	70	28.76	13	1.64	0.65	NO	FTNVD	39	2.9